Original research

Incidence and outcome of perforations during medium vessel occlusion compared with large vessel occlusion thrombectomy

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ABSTRACT

Background Vessel perforation during thrombectomy is a severe complication and is hypothesized to be more frequent during medium vessel occlusion (MeVO) thrombectomy. The aim of this study was to compare the incidence and outcome of patients with perforation during MeVO and large vessel occlusion (LVO) thrombectomy and to report on the procedural steps that led to perforation.

Methods In this multicenter retrospective cohort study, data of consecutive patients with vessel perforation during thrombectomy between January 1, 2015 and September 30, 2022 were collected. The primary outcomes were independent functional outcome (ie, modified Rankin Scale 0–2) and all-cause mortality at 90 days. Binomial test, chi-squared test and *t*-test for unpaired samples were used for statistical analysis.

Results During 25 769 thrombectomies (5124 MeVO, 20 645 LVO) in 25 stroke centers, perforation occurred in 335 patients (1.3%; mean age 72 years, 62% female). Perforation occurred more often in MeVO thrombectomy (2.4%) than in LVO thrombectomy (1.0%, $p<0.001$). More MeVO than LVO patients with perforation achieved functional independence at 3 months (25.7% vs 10.9%, $p=0.001$). All-cause mortality did not differ between groups (overall 51.6%). Navigation beyond the occlusion and retraction of stent retriever/aspiration catheter were the two most common procedural steps that led to perforation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Perforation of an intracranial artery during thrombectomy is a serious adverse event and is associated with poor outcome and death. It is assumed to be more frequent during medium vessel occlusion (MeVO) thrombectomy compared with large vessel occlusion (LVO) thrombectomy, but large studies are lacking.

WHAT THIS STUDY ADDS

⇒ In a retrospective cohort of 25 769 thrombectomies (5124 MeVO, 20 645 LVO), the frequency of vessel perforation in MeVO thrombectomy was approximately twice the frequency observed in LVO thrombectomy and mortality was approximately 50% for both groups.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Interventionalists performing MeVO thrombectomy should make every effort to avoid vessel perforation including the further development and application of safety techniques. The risk of vessel perforation during MeVO thrombectomy should be considered in ongoing randomized trials and in subsequent guidelines.

Conclusions In our cohort, perforation was approximately twice as frequent in MeVO than in LVO thrombectomy. Efforts to optimize the procedure may focus on navigation beyond the occlusion site and retraction of stent retriever/aspiration catheter. Further research is necessary in order to identify thrombectomy candidates at high risk of intraprocedural perforation and to provide data on the effectiveness of endovascular countermeasures.

INTRODUCTION

In 2015, five randomized clinical trials showed an overwhelming benefit of thrombectomy in acute ischemic stroke patients with large vessel occlusion (LVO).[1] Since then, indications for thrombectomy are continuously expanding.[2] However, there is a lack of evidence as to whether patients with acute ischemic stroke due to medium vessel occlusion (MeVO) benefit from thrombectomy. Several randomized trials have been initiated to answer this question, such as DISTAL (EnDovascular Therapy Plus Best Medical Treatment (BMT) vs BMT Alone for MedIum VeSsel Occlusion sTroke, ClinicalTrials.gov Identifier: NCT05029414), DISTALS (Distal Ischemic Stroke Treatment With Adjustable Low-profile Stentriever, NCT05152524), DISCOUNT (Evaluation of Mechanical Thrombectomy in Acute Ischemic Stroke Related to a Distal Arterial Occlusion, NCT05030142) and ESCAPE-MEVO (EndovaSCular TreAtment to imProve outcomEs for Medium Vessel Occlusions, NCT05151172). Arguments against thrombectomy in MeVO include a possibly lower clinical benefit compared with LVO thrombectomy as well as a possibly higher risk of hemorrhage due to (a) thinner vessel walls, (b) higher tortuosity[3] and (c) partial lack of dedicated devices explicitly designed for medium vessels.[4]

Perforation during thrombectomy represents a severe complication and is associated with poor functional outcome or death.[5] However, available data are limited.[6] In medium vessel (MeV) perforation, the maximum flow rate during active extravasation might be lower compared with large vessel (LV) perforation. Therefore, less extravasation might occur until countermeasures are in place. Furthermore, if intentional occlusion of the perforated vessel is deemed necessary, the volume of brain parenchyma that will subsequently suffer from ischemia/infarction is smaller in MeV perforation compared with vessel sacrifice in LV perforation.

The aim of this quality assurance project was to describe the frequency and outcomes of patients with a perforation during MeVO thrombectomy and to compare them to patients with a perforation during LVO thrombectomy.

METHODS

Data of consecutive patients with vessel perforation during thrombectomy (confirmed by extravasation during an angiographic series) were retrospectively collected from multiple stroke centers.

Patient selection

Consecutive patients were included if the corresponding perforation occurred between January 1, 2015 and September 30, 2022 and was confirmed by extravasation during an angiographic series. No other formal inclusion and exclusion criteria were applied. For patients with an intracranial perforation, collected data included baseline characteristics of the patients, neurovascular risk factors, site of occlusion and site of perforation. The procedural step during which perforation occurred was evaluated (multiple choice, options: 1 - access to occlusion, 2 - probing beyond the occlusion, 3 - deployment of stent retriever, 4 - advancement of aspiration catheter, 5 - retraction of stent retriever/aspiration catheter, 6 - contrast injection, 7 - other (specify)). Modified Rankin Scale (mRS) at 90 days was collected as an outcome measure. Independent functional outcome was defined as mRS=0–2. Furthermore, an increase in National Institutes of Health Stroke Scale (NIHSS) score ≥2 points or death within 24 hours after admission were evaluated also. [NB. If a patient died during their hospital stay or was comatose, NIHSS at discharge was defined as 42.]

Ethics committee approval and patient consent were not required according to current local legislation as all data were anonymized before analysis and the project involved assessing safety and quality of routine acute ischemic stroke management in the participating institutions.

Definitions

Following the definitions of the DISTAL trial, LVs were defined as the internal carotid artery (ICA), M1-segment and dominant M2-segment of the middle cerebral artery (MCA; that is, the M2 branch perfusing more than 50% of the MCA territory), the vertebral arteries and the basilar artery.

Table 1 Baseline characteristics

Characteristic	All patients (n=335) n (%)	MeVO (n=124) n (%)	LVO (n=211) n (%)
Age (years, mean±SD)	72.1±13.9	72.6±13.4	71.7±14.3
Gender (female patients)	206/335 (61.5)	74/124 (59.7)	132/211 (62.6)
Arterial hypertension	236/332 (71.1)	90/123 (73.2)	146/209 (69.9)
Obesity	47/265 (17.7)	13/85 (15.3)	34/180 (18.9)
Hyperlipidemia	124/328 (37.8)	46/121 (38.0)	78/207 (37.7)
Diabetes	75/328 (23.0)	32/119 (26.9)	43/207 (20.8)
Atrial fibrillation			
Treated	84/327 (25.7)	38/120 (31.7)	46/207 (22.2)
Untreated	45/327 (13.8)	13/120 (10.8)	32/207 (15.5)
None	198/327 (60.6)	69/120 (57.5)	129/207 (62.3)
Smoking status			
Active smoker	40/236 (16.9)	12/82 (14.6)	28/154 (18.2)
Former smoker	46/236 (19.5)	16/82 (19.5)	30/154 (19.5)
Non-smoker	150/236 (63.6)	54/82 (65.9)	96/154 (62.3)
ICAD at any location	52/321 (16.2)	11/116 (9.5)	41/205 (20.0)
Pre-stroke mRS			
0	209/327 (63.9)	73/122 (59.8)	136/211 (66.3)
1	45/327 (13.8)	16/122 (13.1)	29/211 (14.1)
2	33/327 (10.1)	16/122 (13.1)	17/211 (8.3)
3	30/327 (9.2)	14/122 (11.5)	16/211 (7.8)
4	10/327 (3.1)	3/122 (2.5)	7/211 (3.4)
5	0	0	0
6	0	0	0
NIHSS at admission (mean±SD)	14.2±6.9 (n=326)	13.2±6.3 (n=122)	14.8±7.3 (n=204)

ICAD, intracranial arteriosclerotic disease; LVO, large vessel occlusion; MeVO, medium vessel occlusion; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation.

LVO was defined as occlusion of one or several of the above mentioned LVs. MVs were defined to encompass codominant or nondominant M2-segments, M3- and M4-segments of the MCA as well as the anterior cerebral artery (ACA) and posterior cerebral artery (PCA) and their branches, respectively. MeVO was defined as occlusion of one or several of the above mentioned MVs.

Patients were deemed to belong to the MeVO group if an initial LVO developed to one or several MeVOs before the beginning of thrombectomy. If both LVO and MeVO were present, the patient was assigned to the LVO group if perforation happened during LVO thrombectomy and to the MeVO group if perforation happened during MeVO thrombectomy.

Statistics

We compared the incidence of perforation between MeVO and LVO thrombectomy with the binomial test. Dichotomized variables (incidence of MeV and LV perforation; mRS 0–2, NIHSS increase >2 or death) were compared using the chi-squared test. Ordinal variables (NIHSS at baseline) were compared using the Mann–Whitney U test. The frequencies of the procedural steps during which perforation occurred were compared between MeVO and LVO patients by using the t-test for unpaired samples. All statistical analysis was carried out using SPSS v 28.0.1.0 (IBM SPSS Statistics, Armonk, NY, USA). We deemed p-values <0.05 to be significant.

RESULTS

During 25 769 thrombectomies in 25 stroke centers, perforation with active extravasation occurred in 335 patients (mean age 72.1±13.9 years, range 16–98 years, 61.5% female), corresponding to a perforation rate of 1.3%.

MeVO patients had a lower NIHSS at admission compared with LVO patients (13.2±6.3 vs 14.8±7.3, $p=0.049$; for details of baseline characteristics see table 1).

In 174 cases thrombectomy was carried out in general anesthesia, in 134 cases in conscious sedation and 26 cases were performed with local anesthesia only. In one case no information about the anesthesiologic management was available. A total of 774 endovascular maneuvers were reported including 462 maneuvers with combined aspiration and stent retriever thrombectomy, 204 maneuvers with aspiration thrombectomy alone, 92 maneuvers with stent retriever thrombectomy alone, 6 applications of intraarterial thrombolysis, 9 angioplasties and 1 stenting.

Perforation occurred significantly more often in MeVO thrombectomies (124 perforations in 5124 MeVO thrombectomies, 2.4%) compared with LVO thrombectomies (211 perforations in 20 645 LVO thrombectomies, 1.0%, $p<0.001$). Perforation during MeVO thrombectomy was significantly more often perforation of a MeV (87.9% MeV perforation, 12.1% LV perforation) compared with perforations during LVO thrombectomy (46.0% MeV perforation, 54.0% LV perforation, $p<0.001$; see details in tables 2 and 3). In 149 patients with vessel perforation (87 LVO, 62 MeVO) the vessel perforation was treated by specific endovascular means. These procedures comprised temporary inflation of a balloon guide catheter (n=21), temporary inflation of an intracranial balloon catheter (n=71), temporary coil placement without detachment (n=19), permanent coil occlusion of the perforated vessel (n=67) and other endovascular approaches such as permanent vessel occlusion using a liquid embolic (n=29) or a combination of these methods.

Table 2 Occlusion site (381 occlusions in 335 patients)

Occlusion site	n
ICA	53
Vertebral artery	9
Basilar artery	28
MCA	
M1-segment	128
M2-segment	121
M3-segment	14
M4-segment	1
ACA	
A1-segment	3
A2-segment	10
A3-segment	1
PCA	
P1-segment	13

ACA, anterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.

Overall functional outcome after perforation was poor, with a independent functional outcome at 90 days in 16.1% of all patients and a mortality rate at 90 days of 51.6% (figure 1; details in online supplemental table S1). MeVO patients achieved an independent functional outcome at 90 days significantly more often compared with LVO patients

Table 3 Perforation site (n=334)

Perforation site	All patients (n=334) n (%)	MeVO (n=124) n	LVO (n=210) n
ICA	23 (6.9)	3	20
Vertebral artery	2 (0.6)	0	2
Basilar artery	12 (3.6)	0	12
MCA			
M1-segment	61 (18.2)	6	55
M2-segment	135 (40.3)	61	74
M3-segment	61 (18.2)	38	23
Perforator from M1-segment	5 (1.5)	1	4
ACA			
A1-segment	1 (0.3)	1	0
A2-segment	3 (0.9)	2	1
A3-segment	2 (0.6)	1	1
ACOM	1 (0.3)	1	0
PCA			
P1-segment	18 (5.4)	6	12
P2-segment	2 (0.6)	1	1
P3-segment	1 (0.3)	1	0
PCOM	1 (0.3)	0	1
Perforator from PCA or basilar artery	3 (0.9)	1	2
Anterior choroidal artery	2 (0.6)	0	2
PICA	1 (0.3)	1	0

ACA, anterior cerebral artery; ACOM, anterior communicating artery; ICA, internal carotid artery; LVO, large vessel occlusion; MCA, middle cerebral artery; MeVO, medium vessel occlusion; PCA, posterior cerebral artery; PCOM, posterior communicating artery; PICA, posterior inferior cerebellar artery.

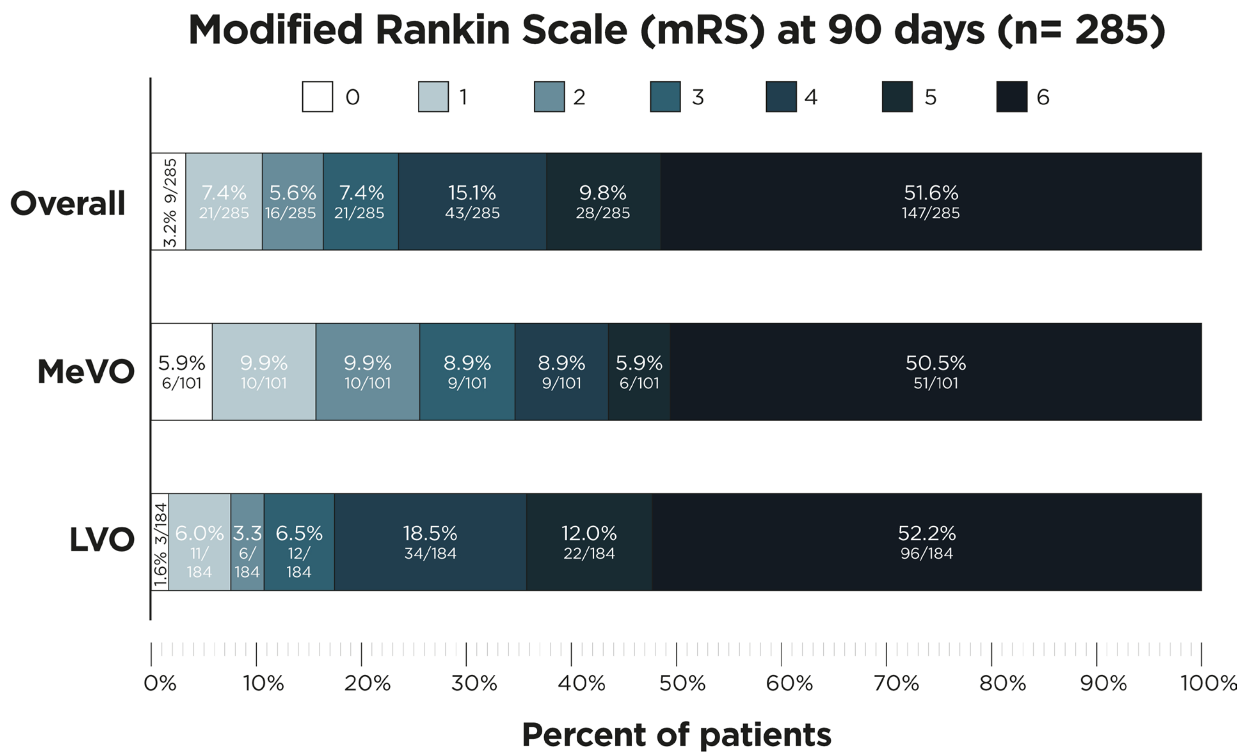

Figure 1 Modified Rankin scale (mRS) at 90 days in patients experiencing perforation during thrombectomy. LVO, large vessel occlusion; MeVO, medium vessel occlusion.

(25.7% in MeVO patients, 10.9% in LVO patients, $p=0.001$). However, mortality at 90 days did not differ between the two groups (50.5% vs 53.0%, $p=0.68$). In MeVO patients, an NIHSS increase of ≥2 points or death within 24 hours after admission occurred significantly less often (52.4% of MeVO patients, 65.4% of LVO patients, $p=0.03$).

For both MeVO and LVO thrombectomies, the two most common procedural steps leading to perforation were navigation beyond the occlusion (30.7% of all perforations) and retraction of stent retriever/aspiration catheter (35.5% of all perforations; details in online supplemental table S2). No significant difference was found between MeVO and LVO thrombectomies regarding the frequency of the different procedural steps that led to perforation.

DISCUSSION

In this large, retrospective, multicenter analysis, perforation with active extravasation during thrombectomy was a rare but severe complication in both MeVO and LVO thrombectomy. Perforation in MeVO thrombectomy occurred approximately twice as frequently compared with LVO thrombectomy. Functional outcome was poor for both patient groups and independent functional outcome was achieved only by 16.1% of patients. In comparison, in a large prospective registry, patients with LVO receiving thrombectomy overall achieved independent functional outcome in 37% of cases.[7] A different registry-based study reported independent functional outcome after thrombectomy in 36% of all LVO patients and 45% of all MeVO patients.[8]

Patients with perforation during MeVO thrombectomy achieved an independent functional outcome more often compared with patients with perforation during LVO thrombectomy. This may be explained in part by lesser stroke severity at stroke onset. Navigation beyond the occlusion and retraction of stent retriever/aspiration catheter were the two procedural steps leading to most perforations in both MeVO and LVO thrombectomies. Our results are in line with smaller previous studies as they reported a frequency of perforations during thrombectomy of between 0.7% and 6.9%.[6 9–12]

This study substantiates the hypothesis that MeVO thrombectomy might be characterized by a higher frequency of perforations.[6] In the majority of MeVO patients the natural course of disease is less severe than in patients with LVO.[13] This might contribute to the finding that patients who survived the perforation more often had an independent functional outcome if the initial occlusion was an MeVO compared with an LVO. However, the impact of perforation during thrombectomy can be considered even greater in MeVO patients since their chances of independent functional outcome without thrombectomy are higher compared with LVO patients.[13]

Perforation during thrombectomy is known to be associated with poor functional outcome and death.[6 9–11] In our study, the frequency of good functional outcome at 90 days for patients with perforation during LVO thrombectomy of 10.9% is lower compared with previous studies. This discrepancy may partially be explained by a less rigorous definition of perforation. Previous studies did not always differentiate between perforations with extravasation on an angiography series as opposed to the finding of subarachnoid blood on postinterventional imaging.[10] We included only cases with a visible extravasation in our study. There are multiple studies showing that subarachnoid hemorrhage on follow-up imaging cannot be directly compared with vessel perforation since it is characterized by a rather benign course.[6 14] Furthermore, previous reports did not systematically differentiate between LVO and MeVO patients.[6 9]

Our study confirms previous work[12] reporting that the two procedural steps harboring the highest risk of perforation

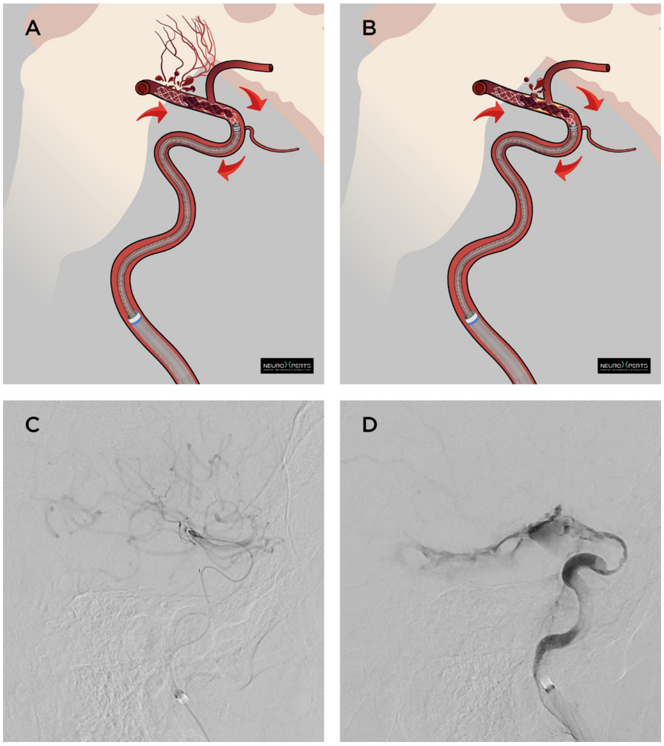

Figure 2 Possible mechanisms of vessel perforation during retraction of stent retriever/aspiration catheter. (A) Rupture of perforator branches due to mechanical shear stress during the retrieval. (B) rupture of the main vessel due to a preexisting atherosclerotic lesion leading to vulnerability. (C) In a patient with acute occlusion of the terminal internal carotid artery at the location of a wall abnormality presumed to be an atherosclerotic plaque (not shown), a microcatheter has been navigated beyond the occlusion. Microcatheter injection in a lateral projection confirms the microcatheter position in the middle cerebral artery. Subsequently, a stent retriever has been deployed and a combined thrombectomy maneuver has been performed. (D) Contrast injection after the thrombectomy maneuver shows active extravasation from the terminal internal carotid artery.

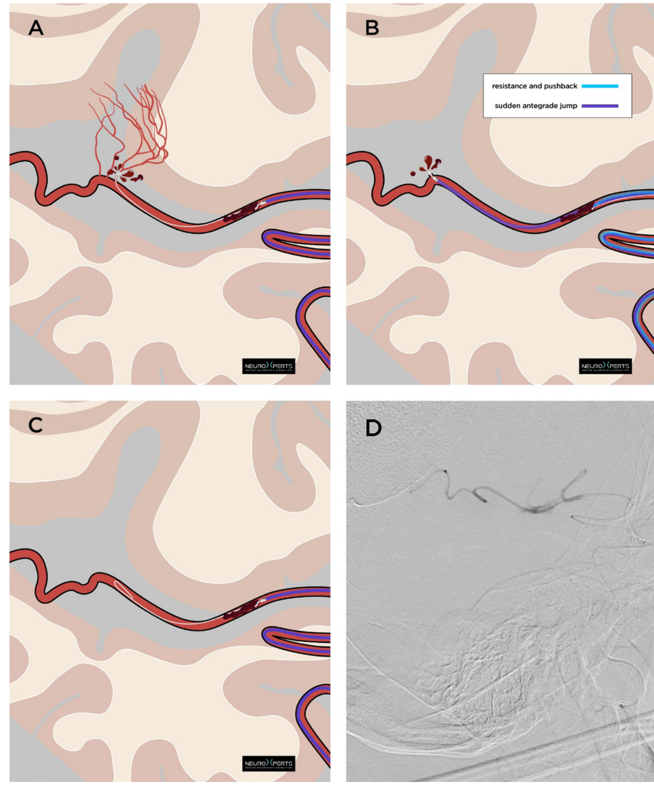

Figure 3 Possible mechanisms of vessel perforation while probing beyond the occlusion. (A) Inadvertent probing in a small caliber branch with the microwire leading to vessel perforation. (B) After passing the occlusion with the microwire, the microcatheter gets stuck at the level of the occlusion, leading to resistance and pushback (light blue). The forward pressure suddenly releases, leading to a sudden antegrade jump of the microcatheter (purple). During this movement, the tip of the microwire perforates the vessel wall. (C) A J-shaped tip of the microwire, sufficient distance between microwire tip and microcatheter tip and microcatheter navigation without excessive forward pressure might decrease the risk of vessel perforation during probing beyond the occlusion. (D) In a patient with an M2-occlusion, the microcatheter has been navigated beyond the occlusion. Digital subtraction angiography in lateral projection with microcatheter injection shows contrast extravasation close to the tip of the microcatheter.

are navigation beyond the occlusion and stent retriever/aspiration catheter retrieval. Figures 2 and 3 illustrate possible mechanisms of vessel perforation during navigation beyond the occlusion and during retrieval of the stent retriever/aspiration catheter. J-configuration of the microwire, soft-tip microcatheters and appropriately sized stent retrievers and aspiration catheters might help to decrease the risk of perforation.[5] Applying intense aspiration within a non-occluded segment on an intracranial artery might lead to luminal collapse and consecutively inadvertent shear forces at the vessel wall, which might increase the risk of vessel perforation.[15] Patient motion might not only lead to perforation but might also affect the detection of contrast extravasation if movement artifacts are encountered during an angiographic run. Performing thrombectomy with general anesthesia might therefore lower the risk of perforation and help in detection and treatment of perforation. One major meta-analysis of patients in randomized trials described a tendency to support this hypothesis,[16] but further studies are needed to answer this question.

Our study has several limitations, namely (a) its retrospective design and (b) the selection of contributing centers based on their willingness to participate, which might limit the study's validity. Outcome data of patients without perforation were not collected. Therefore, direct comparison between the outcome of patients with perforation and the outcome of those without perforation was not feasible. Strengths of our study are (a) the high number of patients and (b) the international multicenter design including centers with different experience in MeVO thrombectomy increasing the generalizability of our results.

In conclusion, perforation with active extravasation during thrombectomy represents a severe complication which frequently results in poor functional outcome or death. Perforation occurred more frequently in MeVO thrombectomy. Mortality at 90 days was similar for MeVO and LVO patients; however, patients with perforation during MeVO thrombectomies more frequently had an independent functional outcome compared with LVO thrombectomy. Navigation beyond the occlusion and retraction of the stent retriever and/or aspiration catheter are the most dangerous procedural steps during thrombectomy according to our data. Further studies with a direct comparison between patients with perforation during thrombectomy and those without perforation might aid in the detection of risk factors for perforation and in the appreciation of the relevance of an intracranial perforation for the patients' outcome.

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Contributors VS-Z had the idea for the study, monitored data collection, collected data, designed the analysis plan, cleaned, analyzed and interpreted the data, and drafted and revised the manuscript. He is guarantor. AB designed the analysis plan, revised the manuscript and approved the final version to be published. NN and NK collected data, cleaned the data, revised the manuscript and approved the final version to be published. IT and KAB cleaned the data, revised the manuscript and approved the final version to be published. MAM, JJ, AC, KK, KA, EM, PM, GS, CR, CHN, IM, AJ, RR, PY, KMF, SQW, DC, AB, DPOK, AC, JSK, JS, NL, LR, SAK, AMS, IF, TR-A, CJM, AB, MM, AL-F, CP-G, CC, MP, JM, FG, WC, CPP, MB, FF, PTK, GE, JH, PM, MK and DW collected data, revised the manuscript and approved the final version to be published. MK and UF interpreted the data, revised the manuscript and approved the final version to be published. M-NP had the idea for the study, designed the analysis plan, interpreted the data, revised the manuscript and approved the final version to be published. He is guarantor.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This retrospective cohort study was a quality assurance project in the participating centers, therefore approval by local ethics committees was not necessary, nor was individual patient consent mandatory. Furthermore, the majority of patients included in the study were either deceased or unable to formulate their will due to neurologic deficits. Thus, obtaining informed consent is likely not feasible in this study population.

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