Original research

Mechanical thrombectomy for acute ischemic stroke in COVID-19 patients: multicenter experience in 111 cases

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ABSTRACT

Background Data on the frequency and outcome of mechanical thrombectomy (MT) for large vessel occlusion (LVO) in patients with COVID-19 is limited. Addressing this subject, we report our multicenter experience.

Methods A retrospective cohort study was performed of consecutive acute stroke patients with COVID-19 infection treated with MT at 26 tertiary care centers between January 2020 and November 2021. Baseline demographics, angiographic outcome and clinical outcome evaluated by the modified Rankin Scale (mRS) at discharge and 90 days were noted.

Results We identified 111 out of 11 365 (1%) patients with acute or subsided COVID-19 infection who underwent MT due to LVO. Cardioembolic events were the most common etiology for LVO (38.7%). Median baseline National Institutes of Health Stroke Scale score and Alberta Stroke Program Early CT Score were 16 (IQR 11.5–20) and 9 (IQR 7–10), respectively. Successful reperfusion (mTICI ≥2b) was achieved in 97/111 (87.4%) patients and 46/111 (41.4%) patients were reperfused completely. The procedure-related complication rate was 12.6% (14/111). Functional independence was achieved in 20/108 (18.5%) patients at discharge and 14/66 (21.2%) at 90 days follow-up. The in-hospital mortality rate was 30.6% (33/108). In the subgroup analysis, patients with severe acute COVID-19 infection requiring intubation had a mortality rate twice as high as patients with mild or moderate acute COVID-19 infection. Acute respiratory failure requiring ventilation and time interval from symptom onset to groin puncture were independent predictors for an unfavorable outcome in a logistic regression analysis.

Conclusion Our study showed a poor clinical outcome and high mortality, especially in patients with severe acute COVID-19 infection undergoing MT due to LVO.

BACKGROUND

Neurological complications during infection with the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are common, ranging from 25% to 80% of patients hospitalized with COVID-19.[1 2] A clear association of acute cerebrovascular disease with COVID-19 has been observed, with an overall pooled incidence of 1.4% in a recent meta-analysis.[3] Acute ischemic stroke (AIS) is the most common manifestation of acute cerebrovascular disease in patients suffering from COVID-19 and is reported as a presenting feature of the young.[3 4] Compared with the pre-pandemic period, younger patients with COVID-19 without vascular risk factors have been undergoing mechanical thrombectomy (MT) for AIS due to large vessel occlusion (LVO).[5 6] Studies suggest that the activation of the coagulation pathway is related to the infection-induced systemic inflammatory response.[7] SARS-CoV-2 enters the blood stream by breaching the blood–air barrier via the lung capillary adjacent to the alveolus. As the blood–air barrier is breached, a cascade of events unfolds including endothelial dysfunction, formation of antiphospholipid antibody complexes promoting platelet aggregation, coagulation cascade, and formation of cross-linked fibrin blood clots, leading to thrombosis and stroke in individuals with COVID-19 infection.[8]

Due to the systemic effect of the coronavirus with hypercoagulation, hyperinflammation and respiratory insufficiency, a poor prognosis and increased mortality among COVID-19 patients treated by MT for LVO must be assumed.[9] Specific characteristics of COVID-19-associated stroke still remain unknown, and data on the frequency and outcome of patients with COVID-19 undergoing MT for AIS are limited.[10]

We aimed to report our multicenter experience with MT in patients with AIS and associated COVID-19 infection, evaluating the angiographic and clinical outcome.

METHODS

We conducted a retrospective study of patients with AIS with laboratory-confirmed acute or subsided (within 6 months) COVID-19 infection who were treated endovascularly at 26 tertiary care centers in Germany and Austria between January 2020 and November 2021. We identified all patients who received MT or were treated with the intention for thrombectomy due to LVO in cerebral arteries including the distal internal carotid artery, middle cerebral artery (M1, M2 and M3), anterior cerebral artery (A1 and A2), distal vertebral artery, basilar artery, and posterior cerebral artery (P1 and P2). A confirmed diagnosis of COVID-19 was defined by a positive laboratory result for SARS-CoV-2 on high-throughput sequencing or reverse transcription PCR assay of nasal and/or oropharyngeal swab specimens.

Demographics, comorbidities, technical features, complications, angiographic and clinical outcomes were noted. The etiology of the occlusion was based on the TOAST classification. There were no limitations on procedural characteristics including the use of different thrombectomy techniques and intra-arterial thrombolysis, which were left to the attending neuroradiologist's discretion. Endovascular treatment was performed with approved MT devices, using stent-retrievers or large-bore aspiration catheters or a combination of both.

Complete reperfusion was defined as a modified Thrombolysis in Cerebral Infarction (mTICI) scale score of 3. Successful reperfusion was defined as mTICI 2b. The clinical efficacy outcome was the rate of functional independence measured by the modified Rankin Scale (mRS) and defined as 0–2 at discharge and 90 days. All National Institutes of Health Stroke Scale (NIHSS) and mRS grades were assessed by a consultant neurologist. Post-interventional symptomatic intracranial hemorrhage (sICH) was graded according to the European Cooperative Acute Stroke Study criteria.[11]

According to the guidelines of the respective local ethics committees, ethical approval was given when necessary for this anonymous retrospective study, which was conducted in accordance with the Declaration of Helsinki. Patient consent for treatment was obtained according to the individual institutional guidelines. Due to the retrospective nature of the study, additional informed consent was deemed unnecessary.

Statistical analysis

Categorical variables are presented as numbers and percentages and compared using the χ^2 and Fisher's exact test, as appropriate. Ordinal variables are presented as median and IQR and compared using the Mann–Whitney U test. Continuous variables are presented as mean with SD and compared using the Student's t-test and Mann–Whitney U test, as appropriate. Factors predictive of an unfavorable outcome (mRS 3–6) at discharge in the univariate analysis ($p<0.05$) were entered into a binary logistic stepwise regression model to identify independent factors for an unfavorable outcome. Independent variables included in the logistic regression analyses were tested for multicollinearity calculating the variance inflation factor (VIF). A VIF >5 was assumed to indicate high multicollinearity between the respective independent variable and the others. In this case, strongly correlating variables were identified and stepwise eliminated until all independent variables had a VIF ≤5. All calculations were performed using SPSS software version 25 (IBM SPSS Statistics for Windows, IBM Corp, Armonk, New York, USA). A p value <0.05 was considered statistically significant.

RESULTS

Of 11 365 patients from 26 tertiary stroke centers screened, 111 patients with acute or subsided COVID-19 infection underwent MT due to LVO between January 2020 and November 2021. The prevalence of MT in COVID-19 patients measured by the case volume of all centers during the inclusion time was 1%.

Baseline characteristics

Out of 111 patients, 97 patients had a laboratory-confirmed diagnosis of acute COVID-19 infection and 14 patients presented after subsided COVID-19 infection. The acute COVID-19 infection was determined during hospitalization, immediately before or after the endovascular thrombectomy, with a reverse transcription PCR test. Patient baseline characteristics are shown in table 1.

Of 97 patients with acute COVID-19 infection, 31 (32%) presented with a severe course requiring intubation due to acute respiratory failure during hospitalization. Mild (without respiratory distress) and moderate (requiring non-invasive ventilation) courses of COVID-19 infection were found in 43 (44.3%) and 23 (23.7%) patients, respectively. The median age was 74 (IQR 63–82) years and 70/111 (63.1%) were male. Seven patients (6.3%) were younger than 50 years.

LVO was localized in the anterior circulation in 101/111 (91%) patients, with most common sites in M1 (51/101; 50.5%) and distal internal carotid artery (25/101; 24.8%), followed by M2 (21/101; 20.8%). Basilar artery occlusion represented 9% (10/111) of cases.

Tandem occlusion occurred in 19/111 (17.1%) patients. In 5/111 (4.5%) cases re-occlusion within 30 days was observed. Of these, three cases of large vessel re-occlusion were localized in the same territory and in two cases a different territory was affected. Intravenous thrombolysis (IVT) was administered in 48/111 (43.2%) patients.

Median baseline NIHSS and ASPECTS were 16 (IQR 11.5–20) and 9 (IQR 7–10), respectively.

The median interval between onset and groin puncture was 220 (IQR 150–290) min. Thirty-nine (35.1%) patients presented as wake-up strokes. The rate of pretreatment functional independence (mRS ≤2) was 73% (81/111).

Cardioembolic cause was the most common etiology for LVO and was found in 43/111 (38.7%) patients, followed by large artery atherosclerosis (22/111; 19.8%). In 11/111 (9.9%) patients other etiology (eg, dissection, infectious) was found. Stroke etiology remained unknown in 34/111 (30.6%) patients.

Procedural and functional outcome

MT was performed under general anesthesia in 100/111 (90.1%) and conscious sedation in 11/111 (9.9%) patients. The median

Table 1 Baseline characteristics of patients with acute or subsided COVID-19 infection undergoing mechanical thrombectomy

	Patients with COVID-19 treated by MT (n=111)
Demographics	
Age (years), median (IQR)	74 (63–82)
Sex (male)	70/111 (63.1%)
COVID-19 infection	
Acute	97/111 (87.4%)
Subsided	14/111 (12.6%)
Respiratory status during hospitalization	
No respiratory distress	31/97 (32%)
Acute respiratory failure requiring non-invasive ventilation	43/97 (44.3%)
Acute respiratory failure requiring intubation	23/97 (23.7%)
Medical history	
Arterial hypertension	78/111 (70.3%)
Atrial fibrillation	39/111 (35.1%)
Diabetes	26/111 (23.4%)
Dyslipidemia	32/111 (28.8%)
Smoking	14/111 (12.6%)
Stroke characteristics	
mRS pre-treatment 2	81/111 (73%)
Baseline NIHSS, median (IQR)	16 (11.5–20)
Baseline ASPECTS, median (IQR)	9 (7–10)
Wake-up stroke	39/111 (35.1%)
Intravenous thrombolysis	48/111 (43.2%)
Onset to groin (min), median (IQR)	220 (150–290)
Site of occlusion	
Distal ICA	25/111 (22.5%)
MCA M1	51/111 (45.9%)
MCA M2	21/111 (18.9%)
MCA M3	1/111 (0.1%)
ACA	3/111 (2.7%)
BA	10/111 (9%)
TOAST	
Large artery sclerosis	22/111 (19.8%)
Cardioembolic	43/111 (38.7%)
Small vessel occlusion	1/111 (0.1%)
Other (infectious)	11/111 (9.9%)
Undetermined	34/111 (30.6%)
Re-occlusion within 30 days	5/111 (4.5%)
Tandem occlusion	19/111 (17.1%)

ACA, anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; min, minutes; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Table 2 Angiographic and clinical outcomes of patients with acute or subsided COVID-19 infection undergoing mechanical thrombectomy

	Patients with COVID-19 treated by MT (n=111)
Angiographic outcomes	
Successful reperfusion (mTICI ≥2b)	97/111 (87.4%)
Complete reperfusion (mTICI 3)	46/111 (41.4%)
First-pass near-complete reperfusion (mTICI 2c/3)	36/111 (32.4%)
First-pass complete reperfusion (mTICI 3)	28/111 (25.2%)
Groin puncture to reperfusion (min), median (IQR)	44 (28–69)
Number of passes, median (IQR)	2 (1–3)
Procedure-related complications	
sICH	6/111 (5.4%)
SAH	9/111 (8.1%)
Intra-arterial dissection	1/111 (0.01%)
Clinical outcomes	
NIHSS at discharge, median (IQR)	13 (4–42)
mRS score 2 at discharge	20/108 (18.5%)
mRS score 2 at 90 days	14/66 (21.2%)
Mortality at discharge	33/108 (30.6%)
Mortality at 90 days	37/66 (56.1%)

min, minutes; mRS, modified Rankin Scale; MT, mechanical thrombectomy; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; SAH, subarachnoid hemorrhage; sICH, symptomatic intracranial hemorrhage.

time interval from groin to final reperfusion was 44 (IQR 28–69) min and the median number of thrombectomy maneuvers was 2 (IQR 1–3) (table 2). The most common first-pass technique was a combined approach with aspiration and stent-retriever thrombectomy in 58/111 (52.3%) patients, followed by aspiration thrombectomy in 46/111 (41.4%) patients. In one patient first-line stent-retriever thrombectomy was performed. Spontaneous recanalization occurred in three cases and in two cases the thrombus localization could not be reached. One patient with intention to MT presented with ventricular fibrillation at the beginning of the endovascular procedure and died eventually of pulmonary artery embolism.

Successful reperfusion was achieved in 97/111 (87.4%) patients and 46/111 (41.4%) patients were reperfused completely. The procedure-related complication rate was 12.6% (14/111). sICH occurred in 6/111 (5.4%) patients. Of these, one patient presented with additional subarachnoid hemorrhage (SAH) and another with iatrogenic intra-arterial dissection. Since the dissection was localized extracranially in the internal carotid artery without hemodynamic relevance, no further treatment was required. Of six patients with sICH, parenchymal hematoma (PH) was found in three cases (2 cases of PH-1 and 1 case of PH-2) and hemorrhagic infarction (HI) was found in three cases (2 cases of HI-1 and 1 case of HI-2). In total, nine patients presented with SAH (8.1%).

Functional independence was achieved in 20/108 (18.5%) patients at discharge and 14/66 (21.2%) at 90 days follow-up. The mortality rate was 30.6% (33/108) at discharge and 56.1% (37/66) at 90 days follow-up. Clinical outcome at discharge and at 90 days was not documented in 3 and 45 patients, respectively.

Clinical outcome of the seven patients under the age of 50 years was mRS 2, mRS 3, mRS 4 in two cases and mRS 6 in two cases. In one patient the clinical outcome was not noted. In two patients one risk factor (smoking) in each case was determined.

Patients with subsided COVID-19 infection showed an increased likelihood of functional independence (at discharge) compared with patients with acute COVID-19 infection (mRS 0–2: 5/14 (35.7%) vs 15/94 (15.5%), p=0.076). In addition, the mortality rate at discharge was lower in patients recovered from COVID-19 compared with patients with acute COVID-19 infection, but without statistical significance (mRS 6: 2/14 (14.3%) vs 31/94 (33%), p=0.16).

In a subgroup analysis, patients with severe acute COVID-19 infection with respiratory failure requiring intubation showed a significantly lower rate of functional independence with significantly higher mortality compared with patients with mild or moderate acute COVID-19 infection (mRS 0–2 at discharge: 0/30 (0%) vs 15/64 (23.4%), p=0.004; mRS 6 at discharge: 15/30 (50%) vs 16/64 (25%), p=0.016).

Univariate and multivariate analyses

We performed univariate and multivariate analyses to identify predictors for an unfavorable outcome (mRS 3–6) at discharge. In the univariate analysis, factors potentially associated with an unfavorable outcome were: no administration of IVT (p=0.001), ventilation (non-invasive or intubation due to respiratory failure, p<0.001), occlusion site in the ICA (p=0.041) or M1 (p=0.001), cardioembolic cause of AIS (p=0.075), higher pre-stroke mRS (p<0.001), tandem occlusion (p=0.021), lower ASPECTS at baseline (p=0.046) or after 24 hours (p=0.001), higher NIHSS at baseline (p=0.002) or at discharge (p<0.001), higher interval time between onset to groin puncture (p=0.042) and lower rates of mTICI 3 (p=0.026). After multicollinearity testing, administration of IVT, ventilation, cardioembolic cause of AIS, ASPECTS at baseline, NIHSS at baseline, interval time between onset to groin puncture and mTICI 3 rates were entered into a binary logistic regression analysis. Ventilation (OR 35.3, 95% CI 2.4 to 523.0; p=0.010) and interval time from onset to groin puncture (OR 1.02, 95% CI 1.00 to 1.04; p=0.016) remained as independent predictors for an unfavorable outcome.

DISCUSSION

We report a large series of patients with COVID-19 infection treated with MT due to LVO focusing on angiographic and clinical outcome. MT in patients with acute or subsided COVID-19 infection remains an infrequent event to date.

Recent studies have reported a prevalence rate of acute stroke in COVID-19 patients of 1.4–1.5%,[3 12] including endovascular treatment due to LVO in about one of four patients (238/1223).[3] These findings correspond with the low incidence and frequency rate of 1% in our study and might be due to several factors. First, our database included patients from 26 different stroke centers with its inherent heterogeneity in the respective populations. Other stroke patients with LVO and COVID-19 might have been admitted to other stroke centers in the various corresponding metropolitan areas. Second, MT in patients with acute severe COVID-19 infection could be complicated by diagnostic delays imposed by the fact that these patients are more likely to be sedated and intubated, thus impeding the early detection of neurological deterioration. Third, the COVID-19 pandemic compromised the application of well-established therapies and appears to be disruptive for acute stroke pathways.[13–15] Stroke patients without respiratory symptoms of COVID-19 might not seek care at all, preferring to stay at home than taking the risk of getting exposed to SARS-CoV-2 at the hospital.

Our patient characteristics in terms of age (median age of 74), baseline NIHSS and ASPECTS are comparable with individual patient data meta-analysis on MT before the pandemic.[16] In contrast, recent small-case series (n <15) have reported that patients with AIS with COVID-19 treated with MT were younger with median ages ranging from 39 to 59.5 years, had higher baseline NIHSS scores (median 17–27) and lower ASPECTS (median 5) at admission.[4 5]

It remains unclear whether the lower rate of young patients in our study (6.3% of patients aged <50 years)—in comparison to results of a recent systematic review which reported a corresponding rate of 17.4% of young patients with AIS with COVID-19[12]—is underestimated due to patients preferring not to enter the hospital at all, as mentioned above.[13]

Our retrospective analysis revealed several findings including high rates of successful and complete final reperfusion of up to 87% and 41%, respectively. The reperfusion rates are in line with recent analyses of MT in patients with COVID-19.[17–19] In addition, the angiographic outcome is comparable to MT studies before the pandemic, suggesting that there is no distinction between MT being performed in an infected or non-infected patient with regard to technical feasibility, safety, and time to flow restoration.[20–22]

This implies that thrombectomy in COVID-19 patients should be pursued with the same extensive effort as in non-infected patients, as these patients may achieve similar good angiographic outcomes. Otherwise, there is a high probability that mortality and functional independence would increase even more.

Most importantly, our study showed the devastating outcome of patients with COVID-19 with AIS due to LVO, even though the reperfusion rates were high. Our results are consistent with another large European multicenter study of MT in COVID-19 patients (n=93)[17] and meta-analyses of AIS patients with COVID-19 infection,[3 12] which reported mortality rates ranging from 29% to 35%. The mortality is therefore twice as high as in the meta-analysis from HERMES (15%).[16] Several aspects related to the COVID-19 infection may explain our findings, including the respiratory distress observed in some patients. Acute respiratory failure requiring non-invasive ventilation or intubation proved to be an independent factor for an unfavorable outcome in multivariate analysis. In fact, mortality was 50% in patients with acute respiratory failure due to COVID-19 infection undergoing MT and comparable to mortality data among COVID-19 patients with acute respiratory distress syndrome in national reports (all countries 39%).[23] Besides, COVID-19 patients with stroke tend to have an elevated incidence of potentially fatal thrombotic complications that could have contributed to the increased risk of death.[12] Indeed, we found a noticeably higher rate of re-occlusion within 30 days compared with a previous analysis of non-infected patients (4.5% vs 0.4%).[24] Re-occlusions might be promoted by a prothrombotic state, antiphospholipid syndrome, cytokine storm or other coagulopathies—factors that have already been described with COVID-19 and related stroke pathogenesis.[25 26]

Notably, patients with subsided COVID-19 infection tend to have a better clinical outcome than patients with acute COVID-19 infection. The mortality in this subgroup of our cohort corresponds to rates of mortality in non-infected stroke patients undergoing MT, indicating that recovered COVID-19 patients should be given separate consideration and stroke pathogenesis might be dissimilar to patients with acute SARS-CoV-2 infection.

Another important factor potentially negatively affecting the clinical outcome of infectious patients treated with MT due to LVO is the significant delay in performing thrombectomy. The median time interval from symptom onset to groin puncture in our study was higher than findings of the German Stroke Registry in 2019 (median 220 min vs 160 min).[27] Additionally, the time interval from onset to groin puncture presented as an independent predictor for an unfavorable outcome in our multivariate analysis. Multiple studies have shown declines in the volumes of MT, IVT and stroke hospitalizations over the pandemic with delays in hospital arrival times and treatment workflow.[28–30]

It is notable that 90% of thrombectomy procedures in our study were performed under general anesthesia. To date, there are no current studies comparing the efficacy of general anesthesia and conscious sedation for MT in patients diagnosed with COVID-19. The decision to intubate for MT must be justified to the patient's need for airway protection and the risk of aerosol exposure to the staff.

It remains unknown whether COVID-19 was primarily responsible for AIS in our study. Cardioembolic etiology for the LVO was found in most patients (38.7%) and could be potentially associated with the systemic hypercoagulability seen in patients with COVID-19. On the other hand, there is no indication of causality as the majority of patients had at least one known stroke risk factor.

An important limitation of our study is the retrospective and multicenter design including attendant selection bias and the use of different thrombectomy equipment and techniques although, notably, the reperfusion rates were high. Furthermore, our study is limited by the fact that the study did not consider a control group of non-infected patients.

CONCLUSIONS

Our study supports the fact that COVID-19 infection is associated with a devastating clinical outcome of patients with AIS due to LVO treated with MT. Patients with acute severe COVID-19 infection and respiratory failure tend to have the highest rate of mortality.

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