

European Multicenter Study of ET-COVID-19

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Abstract

Background and Purpose: Acute ischemic stroke and large vessel occlusion can be concurrent with the coronavirus disease 2019 (COVID-19) infection. Outcomes after mechanical thrombectomy (MT) for large vessel occlusion in patients with COVID-19 are substantially unknown. Our aim was to study early outcomes after MT in patients with COVID-19.

Methods: Multicenter, European, cohort study involving 34 stroke centers in France, Italy, Spain, and Belgium. Data were collected between March 1, 2020 and May 5, 2020. Consecutive laboratory-confirmed COVID-19 cases with large vessel occlusion, who were treated with MT, were included. Primary investigated outcome: 30-day mortality. Secondary outcomes: early neurological improvement (National Institutes of Health Stroke Scale improvement ≥ 8 points or 24 hours National Institutes of Health Stroke Scale 0–1), successful reperfusion (modified Thrombolysis in Cerebral Infarction grade $\geq 2b$), and symptomatic intracranial hemorrhage.

Results: We evaluated 93 patients with COVID-19 with large vessel occlusion who underwent MT (median age, 71 years [interquartile range, 59–79]; 63 men [67.7%]). Median pretreatment National Institutes of Health Stroke Scale and Alberta Stroke Program Early CT Score were 17 (interquartile range, 11–21) and 8 (interquartile range, 7–9), respectively. Anterior circulation acute ischemic stroke represented 93.5% of cases. The rate modified Thrombolysis in Cerebral Infarction 2b to 3 was 79.6% (74 patients [95% CI, 71.3–87.8]). Thirty-day mortality was 29% (27 patients [95% CI, 20–39.4]). Early neurological improvement was 19.5% (17 patients [95% CI, 11.8–29.5]), and symptomatic intracranial hemorrhage was 5.4% (5 patients [95% CI, 1.7–12.1]). Patients who died at 30 days exhibited significantly lower lymphocyte count, higher levels of aspartate, and LDH (lactate dehydrogenase). After adjustment for age, initial National Institutes of Health Stroke Scale, Alberta Stroke Program Early CT Score, and successful reperfusion, these biological markers remained associated with increased odds of 30-day mortality (adjusted odds ratio of 2.70 [95% CI, 1.21–5.98] per SD-log decrease in lymphocyte count, 2.66 [95% CI, 1.22–5.77] per SD-log increase in aspartate, and 4.30 [95% CI, 1.43–12.91] per SD-log increase in LDH).

Conclusions: The 29% rate of 30-day mortality after MT among patients with COVID-19 is not negligible. Abnormalities of lymphocyte count, LDH and aspartate may depict a patient's profiles with poorer outcomes after MT.

Introduction

Incidences of acute ischemic stroke (AIS) among coronavirus disease 2019 (COVID-19) patients has been reported between 1% and 3% in recent retrospective studies.^{1,2} Reports suggested that patients with COVID-19 might be at risk of thromboembolic events caused by abnormalities of coagulation.³ Despite that it should be proved whether these patients are at a higher risk of AIS with large vessel occlusion (LVO), it is conceivable that AIS and LVO might be concurrent with the COVID-19 disease, given the considerable spread of the infection in the world population. Scant data are available about clinical and neurological outcomes of patients infected with the severe acute respiratory syndrome coronavirus (SARS-CoV-2) and developing AIS with LVO, necessitating endovascular treatment with mechanical thrombectomy (MT).^{4–6} Given the systemic impact of the virus with respiratory insufficiency, coagulopathy, and alterations of the immune system and inflammation,^{7–9} higher morbidity and mortality risk could be expected in patients with COVID-19 undergoing MT for LVO.

The aim of this multicenter, European study (the ET-COVID-19 study [Endovascular Thrombectomy in COVID-19 Patients]) was to investigate the efficacy and safety of MT within the first 30 days in patients with AIS and LVO and associated COVID-19 infection.

Methods

Study Design and Study Cohort

Data are available from the corresponding author on reasonable request. The ET-COVID-19 study was a multicenter, European, cohort registry designed to investigate clinical and treatment-related early outcomes after MT for AIS in patients with COVID-19. This study was conducted in 34 high-volume Comprehensive Stroke Centers in 4 European countries (France, Italy, Spain, and Belgium). The Institutional Review Board of Montpellier University Hospital approved this analysis (Institutional Review Board number: RB-MTP_2020_05_202000506). Between March 1, 2020 and May 5, 2020, consecutive AIS patients, with COVID-19 infection and LVO, who underwent MT, were prospectively included in this study.

Patients fulfilling the following criteria were included (1) patients admitted to a Comprehensive Stroke Centers for an AIS and LVO (in the anterior or posterior circulation) who were treated with MT; and (2) a laboratory-confirmed diagnosis of SARS-CoV-2 infection, based on the World Health Organization guidance.⁸ A confirmed case of COVID-19 was defined by a positive laboratory result for SARS-CoV-2 on high-throughput sequencing or reverse transcription polymerase chain reaction assay of nasal oropharyngeal swab specimens.

Data Sources and Data Collection

The site investigators gathered the data from prospectively local databases. Each record was checked independently by 2 clinicians in every hospital center. A deidentified database was filled by experienced neurologists and interventional neuroradiologists. Written informed consent was obtained in every participating center. From each included patient, the following data were recorded: (1) baseline patient demographics and medical history (age, sex, hypertension, diabetes, dyslipidemia, tobacco use, cardiac disease, malignancy, chronic kidney disease, antithrombotic or anticoagulant medication); (2) severity of stroke, assessed with the admission National Institutes of Health Stroke Scale (NIHSS; performed by a certified neurologist) and imaging assessment (performed by a certified radiologist; Alberta Stroke Program Early CT Score [ASPECTS], location of intracranial occlusion, and prestroke modified Rankin Scale); (3) symptoms of COVID-19 infection at the moment of the hospitalization; (4) laboratory testing (performed according to the clinical care needs of the patients) recorded within 48 hours after hospital admission (complete blood cell count, blood chemical analysis, coagulation testing, assessment of liver and renal function, C-reactive protein, and LDH [lactated dehydrogenase]); (5) treatment details (intravenous thrombolysis, anesthesia management, thrombectomy strategy, time delays, angiographic results, treatment-related complications); and (6) postprocedural and 30-day outcome data.

Endovascular Procedure and COVID-19 Patient's Management

Procedures on patients with COVID-19 were performed according to the local hospital guidelines. Patients always wore a surgical mask. A chest computerized tomography was performed either during initial cerebral imaging or soon after. During intervention, all staff wore goggles/face protective shield and a high-protection mask (N95/FFP2/FFP3). Laboratory-confirmed cases of COVID-19 infection were transferred into a dedicated COVID-19 ward/department.

Patients were treated with contact aspiration, stent retriever, or SOLUMBRA strategies as the first-line of intervention. The choice of anesthesia technique (conscious sedation or general anesthesia) was left at the discretion of the operators. Protocols for choosing the type of anesthesia was heterogeneous among the included centers and was based on the need of airway protection in more severe patients, as well as the risk of operator exposition to the SARS-CoV-2 virus. Periprocedural treatment-related complications (embolization in a new territory [defined as an angiographic occlusion in a previously unaffected vascular territory observed on the angiogram after clot removal], arterial dissection/perforation, vasospasm, subarachnoid hemorrhage, and groin puncture hematoma requiring treatment) were evaluated and recorded by two investigators in each center. Non-neurological adverse events occurring within 30 days were recorded either in the Stroke Unit, or in the intensive care unit (ICU), and were classified in cardiac, respiratory, renal, multiorgan, and coagulation dysfunctions.

Outcomes Measures

The primary outcome of this study was the mortality at 30 days after MT.

Secondary outcomes included the following: (1) NIHSS score at 24 hours, early neurological improvement (ENI; defined as NIHSS improvement ≥ 8 points or a total NIHSS 0–1 at 24 hours¹⁰), and early neurological deterioration (defined as a 24 hours worsening ≥ 4 points of the NIHSS); (2) rates of successful and complete reperfusion (defined as a modified Thrombolysis in Cerebral Infarction [mTICI] grade $\geq 2b$ and mTICI grade 3, respectively¹¹); (3) rate of first pass effect defined as mTICI3 grade $\geq 2b$ after first pass; and (4) intracranial hemorrhage (ICH; classified according to European Cooperative Acute Stroke Study II¹²), and symptomatic ICH (acute ICH with an increase in NIHSS ≥ 4 points¹³).

Statistical analysis

Continuous variables are expressed as means $\pm$ SD or medians (interquartile range [IQR]) and categorical variables are expressed as numbers (percentage). Normality of distributions was assessed using histograms and the Shapiro-Wilk test. The overall rates of binary outcomes (30-day all-cause mortality, successful and complete reperfusion, first pass effect, any procedure-related complications, ENI and early neurological deterioration, access to ICU, any ICH, and any non-neurological adverse events within 30 days) were reported with their 95% CIs estimated by using the exact Clopper-Pearson method. Bivariate comparisons in biological markers between survival and nonsurvival patients were done using Student t test in cases of normal distributions or using the Mann-Whiney U test otherwise. For the 3 significant biomarkers (lymphocyte, aspartate, and LDH), we used multivariable logistic regression models to adjust the associations on prespecified confounders (age, initial NIHSS, ASPECTS, and successful reperfusion status) after applying a log-transformation for the 3 biomarkers; odds ratio of mortality per SD change in log-transformed biomarkers values were derived as effect sizes. Statistical testing was performed at the 2-tailed α level of 0.05. No corrections for multiple testing were done regarding the exploratory nature of the present study and results should be interpreted with caution and as hypothesis-generating. Data were analyzed using the SAS software package, release 9.4 (SAS-Institute, Cary, NC).

Results

Study population

Among 855 MT performed during the study period, 93 (10.8%) had a laboratory-confirmed diagnosis of COVID-19 (median age, 71 years [IQR, 59–79]; 63 men [67.7%]) and were included in this study (Figure). Baseline characteristics are reported in Table 1. The most common symptoms of COVID-19 disease were dry cough (40 [43%]), fever (31 [33.3%]), and dyspnea (31 [33.3]; Table I in the Data Supplement). The COVID-19 status was determined during the hospitalization, immediately after the endovascular thrombectomy, with a reverse transcription polymerase chain reaction test.

Median baseline NIHSS and ASPECTS were 17 (IQR, 11–21) and 8 (IQR, 7–9), respectively. Overall, 83 (89.2%) patients presented prestroke modified Rankin Scale score of 0 to 2, whereas 10 (10.8%) had a modified Rankin Scale score of 3. AIS in the anterior circulation represented 93.5% of the included cases (83 patients), and the most common sites of occlusion were M1 (46 [49.5%]) and M2 (16 [17.2%]), followed by the carotid terminus (13 [14%]). Tandem occlusion occurred in 9 patients (9.7%), isolated extracranial internal carotid artery occlusion in 2 patients (2.2%), and anterior cerebral artery occlusion in one (1.1%). Basilar artery occlusion represented 6.5% of cases (6 patients).

Biological data

Laboratory findings were recorded within 48 hours after hospital admission (Table II in the Data Supplement). All the investigated biological data were within normal ranges, except for the following: mean hemoglobin (13g/dL [SD±1.7]) and mean hematocrit (38.5% [SD±7.2]) were slightly lower in male patients compared with normal ranges; median LDH (347 IU [IQR, 224–450]), median C-reactive protein (15.5 mg/L [IQR, 4–40]), median D-dimer (2440 ng/mL [IQR, 920–5250]), mean prothrombin time (13.7 s [SD±2.1]), and mean fibrinogen (4 g/L [SD±2.2]) were higher compared with normal ranges.

Treatment Details and Clinical Outcomes Within 30 days

MT was performed under general anesthesia in 37 (39.8%) cases. Of them, 17 (18.3%) remained intubated at 24 hours after MT, whereas 11 (10.7%) required intubation and ICU management after the MT and within the first 3 days. Intravenous thrombolysis was administered in 36 (38.7%) patients. The rates of successful (mTICI 2b–3) and complete recanalization (mTICI 3) were 79.6% (74 patients [95% CI, 71.3–87.8]), and 43% (40 patients [95% CI, 32.7–53.7]), respectively. First pass effect was achieved in 31 cases (35.2% [95% CI, 25.3–46.2]; Table 2). Median time from symptom onset to groin puncture was 240 minutes (IQR, 180–330); median time from groin puncture to reperfusion was 37 minutes (IQR, 27–60); and median time from symptom onset to successful recanalization was 295 minutes (IQR, 242–392; details in Table III in the Data Supplement and Table 2).

Procedure-related complication rate was 15% (14 patients [95%CI, 8.6%–24.5%]; Table 2). Mortality at 30 days was 29% (27 patients [95%CI, 20–39.4]), and 28 patients (30.1% [95%CI, 21–40.5]) required hospitalization in the ICU. The primary cause of mortality was neurological (associated with ICH or malignant cerebral infarction/edema) in 14 patients (15.1% [95% CI, 8.5–24]) and non-neurological (respiratory failure and multiorgan failure) in 13 patients (14% [95% CI, 8.2–22.6]). The median NIHSS at 24 hours was 14 (IQR, 5–20). Fourteen patients (15.1% [95% CI, 8.5–24]) experienced malignant cerebral infarction, 2 underwent a decompressive craniectomy (2.1% [95% CI, 1.2–7.9]), whereas rates of ICH and symptomatic ICH were 24.7% (23 patients [95% CI, 16.3–34.8]) and 5.4% (5 patients [95% CI, 1.7–12.1]), respectively. At 24 hours after MT, ENI and early neurological deterioration were detected in 19.5% (17 patients [95% CI, 11.8–29.5]) and 18.4% (16 patients [95% CI, 11.5–27.9]) of patients, respectively.

Overall, 25 patients (26.9% [95% CI, 18.2–37.1]) reported non-neurological adverse events within 30 days, and the most common complications were respiratory failure (7 patients [7.5%]), heart failure or acute myocardial infarction (5 patients [5.4%]), and deep venous thrombosis (4 patients [4.3%]).

Comparison of Biological Data Assessed Within 48 Hours of Admission Between Patients Alive and Dead at 30 Days

Table 3 shows laboratory findings in patients alive and dead at 30 days. Patients who died at 30 days exhibited significantly lower levels of lymphocytes (median lymphocyte count/mm³, 900 [IQR, 605–1326] versus 1325 [IQR, 930–2000]), significantly higher levels of aspartate (median IU/L of aspartate, 52 [IQR, 32–55] versus 26 [IQR, 20–37]), and LDH (median IU/L of LDH, 503 [IQR, 376–787] versus 271 [IQR, 207–399]). After adjustment for age, initial NIHSS score, ASPECTS, and successful reperfusion status, these 3 biological markers remained associated with an increased risk of 30-day mortality with an adjusted odds ratio of 2.70 (95% CI, 1.21–5.98) per SD-log decrease in lymphocyte count, 2.66 (95% CI, 1.22–5.77) per SD-log increase in aspartate and 4.30 (95% CI, 1.43–12.91) per SD-log increase in LDH.

Discussion

During the SARS-CoV-2 outbreak, pooling data from three highly affected European countries, our multicenter study elucidated several important findings about the safety and efficacy of the MT for LVO among patients with COVID-19. Overall, 11% of patients with LVO, who underwent MT, were found to be infected with COVID-19. Compared with large randomized controlled trials and individual patient data meta-analysis on MT,^{14,15} this European cohort of patients with COVID-19 appeared to be comparable in terms of age (median age of 71 years), baseline NIHSS, and ASPECTS (respectively 17 and 8). About 67% of LVO in our COVID-19 population was located in the MCA, with only 6.5% of posterior circulation strokes: this was, in general, not dissimilar to what was reported in the overall population harboring LVO.^{15,16} Our study was in contrast with what has been reported in recent small case-series of MT in patients with COVID-19. Escalard et al⁴ described 10 consecutive patients with SARS-CoV-2 infection and AIS treated with MT: patients were young (median age of 59.5), with a severe neurological presentation (median NIHSS 22) and large infarct cores (median ASPECTS, 5). However, data from

published small series are heterogeneous, with median ages ranging from 40 to 69 years^{5,6,17} and median NIHSS scores between 17 and 27.^{6,12}

It is interesting to note that in our population, about 40% of patients with COVID-19 were treated under general anesthesia, and this rate was quite comparable to what was reported in major clinical trials.^{14,18} These results are important because the decision whether to intubate a patient with COVID-19 for MT must balance the patient's need for airway protection and the risk to staff performing the intubation/extubation due to the aerosol generating procedures.¹⁹

Recent reports investigated the impact of the COVID-19 outbreak on the efficiency of the prehospital care chain response and the consequences on care delays for patients with AIS eligible for MT. A French national-level data collection performed between February 15, 2020 and March 30, 2020 revealed an overall 20.9% drop in patients receiving MT, and a significant increase in delays between imaging and groin puncture (mean 144.9 minutes), compared to pre-COVID-19 periods (mean 126.2 minutes). Contrariwise, symptoms-onset to imaging, and symptoms-onset to needle were found comparable to preoutbreak periods.²⁰ Similar findings were reported in a US study that underlined marked delays between symptoms-onset and time of presentation to the hospital.²¹ Interestingly, although our study was not designed to compare outbreak and preoutbreak periods, we found treatment-delays quite comparable to what was reported in previous large randomized controlled trials,^{14,18,22} with a median symptom onset to groin puncture, and groin puncture to successful recanalization of 240 minutes and 37 minutes, respectively.

More importantly, our multicenter study showed poor prognosis of patients with AIS with LVO and SARS-CoV-2 infection. Although successful recanalization was obtained in roughly 80% of patients, the 19.5% rate of ENI at 24 hours was considerably lower compared with the 50% to 80% rates reported in the literature of patients without COVID-19.^{18,23,24} In addition, the combination of AIS and SARS-CoV-2 infection resulted in 29% rate of 30-day mortality. In the meta-analysis from the HERMES collaborators, the 90-day mortality was roughly 15%.¹⁵ This poor prognosis was not explained by known predictive factors of poor outcome (age, baseline NIHSS, and ASPECTS), who were close to those of randomized controlled trials, but it was likely determined by the morbidity and mortality related to the COVID-19 infection. Indeed, ≈27% of patients in our study experienced non-neurological complications, as respiratory and cardiac failure, deep venous thrombosis, pulmonary coinfection, multiorgan failure, and about 1 out of 3 patients required ICU management. In general, rates of mortality of patients with COVID-19 depend on the severity of the disease, patient's comorbidities, age, and laboratory findings. Zhou et al⁸ provided details on the clinical course of 191 hospitalized patients with COVID-19, reporting 28% rate of mortality, with higher median age (69 years versus 52 years), higher Sequential Organ Failure Assessment score, and elevated d-dimer among nonsurvivors. In the study of Zhou et al,⁸ in-hospital mortality was higher than in other reports showing mortality rates between 5% and 20%.^{8,25} In general, despite differences in mortality rates that can be partially related to differences in severity of the disease and length of follow-up,²⁶ several studies showed the association between coagulation, immune, and inflammatory abnormalities and the risk of severe disease and death.^{3,8} In line with these observations, we found that lower values of lymphocyte count, and higher levels of aspartate and LDH were significantly associated with 30-day mortality after MT on COVID-19 population, independent from age, initial ASPECTS, NIHSS scores, and successful reperfusion. Furthermore, we investigated the association between general anesthesia and 30-day mortality, and there was not a significant difference in mortality rate between

patients treated with or without general anesthesia (35.1% [13/37] versus 25.0% [14/56], $P=0.29$). In addition to the assessment of the initial neurological severity, these identified biomarkers can be easily used to distinguish patients with COVID-19 with a more severe condition and higher risk of mortality after MT. Elevated LDH and lower lymphocytes count have been described in several studies as predictors of mortality of patients with COVID-19.^{7,9} Increased LDH reflects tissue and cell damage, and it is an important marker of lung injury in pulmonary interstitial diseases.²⁷ Lymphocytopenia has been documented in severe patients, and it may be related to cytokine storm causing lymphocyte apoptosis and inhibition of lymphocyte proliferation. In addition, interstitial inflammatory infiltrates, dominated by lymphocyte cells, has been documented in SARS-CoV-2 infection, and it may be associated with alveolar injury, and persistent lymphopenia.⁹ Finally, several reasons may explain the predicting value of mortality of elevated concentration of blood aspartate: liver injury caused by antiviral, antibiotics, and anti-inflammatory treatments in more complicated patients; hypoxia/reperfusion liver injury, or multiorgan dysfunction and a potentially direct infection of bile duct cells through the angiotensin-converting enzyme 2 receptor.²⁸

Strengths and Limitations

The strength of our study lies in the multicentric design and in the relatively large sample of patients with COVID-19 having MT and prospectively included in the outbreak period. Accordingly, this is the first and largest study providing data about the safety and efficacy of the MT among the COVID-19 population. In terms of limitation, reporting early results, our study was not designed to investigate functional independence at 3 months. In addition, heterogeneity between different centers concerning treatment-management of patients with AIS should be considered. Finally, the design of the study did not consider a control group of noninfected patients.

Conclusions

Our study provides evidence that SARS-CoV-2 infection has a prominent negative impact on early clinical outcomes of patients with AIS and LVO treated with MT. These patients present a low chance of ENI and a high rate of 30-day mortality. Importantly, abnormalities of lymphocyte count, LDH and aspartate may depict patient's profiles with a more severe infection and poorer outcomes after MT. Further analysis of this multicentric, European registry is needed to investigate the efficacy of the MT on functional outcomes at 3 months in COVID-19 population.

Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
ASPECTS	Alberta Stroke Program Early CT Score
ICH	intracranial hemorrhage

ICU	intensive care unit
IQR	interquartile range
LDH	lactate dehydrogenase
LVO	large vessel occlusion
MT	mechanical thrombectomy
mTICI	modified Thrombolysis in Cerebral Infarction
NIHSS	National Institutes of Health Stroke Scale
SARS-CoV-2	severe acute respiratory syndrome coronavirus

References

1. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, Chang J, Hong C, Zhou Y, Wang D, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 2020;77:683–690. doi: 10.1001/jamaneurol.2020.1127
2. Yaghi S, Ishida K, Torres J, Mac Grory B, Raz E, Humbert K, Henninger N, Trivedi T, Lillemoe K, Alam S, et al. SARS-CoV-2 and stroke in a New York Healthcare System. *Stroke.* 2020;51:2002–2011. doi: 10.1161/STROKEAHA.120.030335
3. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol.* 2020;7:e438–e440. doi: 10.1016/S2352-3026(20)30145-9
4. Escalard S, Maier B, Redjem H, Delvoye F, Hebert S, Smajda S, Cicco G, Desilles JP, Mazighi M, Blanc R, et al. Treatment of acute ischemic stroke due to large vessel occlusion with covid-19: experience from paris. *Stroke.* 2020;51:2540–2543. doi: 10.1161/STROKEAHA.120.030574
5. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, De Leacy RA, Shigematsu T, Ladner TR, Yaeger KA, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N Engl J Med.* 2020;382:e60. doi: 10.1056/NEJMc2009787
6. Wang A, Mandigo GK, Yim PD, Meyers PM, Lavine SD. Stroke and mechanical thrombectomy in patients with COVID-19: technical observations and patient characteristics. *J Neurointerv Surg.* 2020;12:648–653. doi: 10.1136/neurintsurg-2020-016220
7. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, Li Y, Guan W, Sang L, Lu J, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with Covid-19. *JAMA Intern Med.* 2020;180:1081–1089. doi: 10.1001/jamainternmed.2020.2033
8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in

- Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3
9. Yan L, Zhang H-T, Goncalves J, Xiao Y, Wang M, Guo Y, et al. An interpretable mortality prediction model for Covid-19 patients. *Nat Mach Intell*. 2020;2:283–288.
 10. Saposnik G, Di Legge S, Webster F, Hachinski V. Predictors of major neurologic improvement after thrombolysis in acute stroke. *Neurology*. 2005;65:1169–1174. doi: 10.1212/01.wnl.0000180687.75907.4b
 11. Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, Marks MP, Prabhakaran S, Kallmes DF, Fitzsimmons BF, 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
 12. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, Larrue V, Bluhmki E, Davis S, Donnan G, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. *Lancet*. 1998;352:1245–1251. doi: 10.1016/s0140-6736(98)08020-9
 13. Berger C, Fiorelli M, Steiner T, Schäbitz WR, Bozzao L, Bluhmki E, Hacke W, von Kummer R. Hemorrhagic transformation of ischemic brain tissue: asymptomatic or symptomatic? *Stroke*. 2001;32:1330–1335. doi: 10.1161/01.str.32.6.1330
 14. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, 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
 15. Román LS, Menon BK, Blasco J, Hernández-Pérez M, Dávalos A, Majoie CBLM, Campbell BCV, Guillemin F, Lingsma H, Anxionnat R, et al; HERMES Collaborators. Imaging features and safety and efficacy of endovascular stroke treatment: a meta-analysis of individual patient-level data. *Lancet Neurol*. 2018;17:895–904. doi: 10.1016/S1474-4422(18)30242-4
 16. Mattle HP, Arnold M, Lindsberg PJ, Schonewille WJ, Schroth G. Basilar artery occlusion. *Lancet Neurol*. 2011;10:1002–1014. doi: 10.1016/S1474-4422(11)70229-0
 17. Beyrouti R, Adams ME, Benjamin L, Cohen H, Farmer SF, Goh YY, Humphries F, Jäger HR, Losseff NA, Perry RJ, et al. Characteristics of ischaemic stroke associated with COVID-19. *J Neurol Neurosurg Psychiatry*. 2020;91:889–891. doi: 10.1136/jnnp-2020-323586
 18. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, Yan B, Dowling RJ, Parsons MW, Oxley TJ, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792
 19. Smith MS, Bonomo J, Knight WA, Prestigiacomo CJ, Richards CT, Ramser E, Adeoye O, Bertsch S, Shirani P, Vagal A, et al. Endovascular therapy for patients with acute ischemic stroke during the COVID-19 pandemic: a proposed algorithm. *Stroke*. 2020;51:1902–1909. doi: 10.1161/STROKEAHA.120.029863

20. Kerleroux B, Fabacher T, Bricout N, Moise M, Testud B, Vingadassalom S, Ifergan H, Janot K, Consoli A, Hassenet WB, et al. Mechanical thrombectomy for acute ischemic stroke amid the covid-19 outbreak: decreased activity, and increased care delays. *Stroke*. 2020;51:2012–2017. doi: 10.1161/STROKEAHA.120.030373
21. Schirmer CM, Ringer AJ, Arthur AS, Binning MJ, Fox WC, James RF, Levitt MR, Tawk RG, Veznedaroglu E, Walker M, et al; Endovascular Research Group (ENRG). Delayed presentation of acute ischemic strokes during the COVID-19 crisis. *J Neurointerv Surg*. 2020;12:639–642. doi: 10.1136/neurintsurg-2020-016299
22. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, Guillemin F; THRACE Investigators. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. *Lancet Neurol*. 2016;15:1138–1147. doi: 10.1016/S1474-4422(16)30177-6
23. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, San Román L, Serena J, Abilleira S, Ribó M, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. doi: 10.1056/NEJMoa1503780
24. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, et al; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
25. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507–513. doi: 10.1016/S0140-6736(20)30211-7
26. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. *Lancet*. 2020;395:1014–1015. doi: 10.1016/S0140-6736(20)30633-4
27. Kishaba T, Tamaki H, Shimaoka Y, Fukuyama H, Yamashiro S. Staging of acute exacerbation in patients with idiopathic pulmonary fibrosis. *Lung*. 2014;192:141–149. doi: 10.1007/s00408-013-9530-0
28. Gu X, Li X, An X, Yang S, Wu S, Yang X, Wang H. Elevated serum aspartate aminotransferase level identifies patients with coronavirus disease 2019 and predicts the length of hospital stay. *J Clin Lab Anal*. 2020;34:e23391. doi: 10.1002/jcla.23391

Table 1. Baseline Characteristics of the Patients With COVID-19 Treated by Thrombectomy (N=93)

	N.	Values
Demographics		
Age, y	93	71 (59–79)
Male Sex	93	63 (67.7)
Medical history		
Hypertension	93	62 (66.7)
Hypercholesterolemia	93	28 (30.1)
Diabetes	93	20 (21.5)
Smoking	93	21 (22.6)
Previous smoking		17 (18.3)
Active smoking		9 (9.7)
Cardiovascular disease	93	43 (46.2)
Kidney disease	93	4 (4.3)
Cancer	93	15 (16.1)
Antithrombotic medications	93	43 (46.2)
Anticoagulants		21 (22.6)
Antiplatelets		24 (25.8)
Stroke characteristics		
Prestroke mRS	93	
0		72 (77.4)
1		11 (11.8)
≥2		10 (10.8)
Pretreatment NIHSS score	93	17 (11–21)
Wake-up stroke	93	17 (18.3)
Site of occlusion	93	
MCA M1		46 (49.5)
MCA M2		16 (17.2)
T carotid		13 (14.0)
Isolated extracranial ICA		2 (2.2)
Tandem occlusion		9 (9.7)
VB		6 (6.5)
ACA		1 (1.1)
Left hemisphere involvement	93	43 (46.2)
Pretreatment ASPECTS*	93	8 (7–9)
< 6		14 (15.1)

Values are n (%) or median (IQR) unless otherwise as indicated. ACA indicates anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; COVID-19, coronavirus disease 2019; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Score; and VB, vertebrobasilar.

* For posterior circulation occlusions pc-ASPECTS (posterior fossa ASPECT) has been used.

Table 2. Treatment-Related and Clinical Outcomes of Patients With COVID-19 Treated by Thrombectomy (N=93)

	N.	Values	95% CI
Angiographic outcomes			
Successful recanalization (mTICI 2b–3)	93	74 (79.6)	71.3–87.8
Complete recanalization (mTICI 3)	93	40 (43.0)	32.7–53.7
No. of passages	88	2 (1–3)	
First pass effect*	88	31 (35.2)	25.3–46.2
Groin puncture–reperfusion time, min†	73	37 (27–60)	
Procedure-related complications			
Any procedure-related complication	91	14 (15.4)	8.6–24.5
Vessel perforation		5 (5.5)	
Embolism in a new territory		4 (4.4)	
Vasospasm		1 (1.1)	
Groin puncture hematoma requiring treatment		1 (1.1)	
Vessel dissection		3 (3.3)	
Clinical and neurological outcomes within 30 d			
30-day mortality	93	27 (29.0)	20.0–39.4
Primary cause of mortality	93		
Neurological		14 (15.1)	8.5–24.0
Non-neurological		13 (14)	8.2–22.6
Malignant cerebral infarction	93	14 (15.1)	8.5–24.0
Reocclusion of the same artery	93	2 (2.2)	ND
NIHSS at 24 h	87	14 (5–20)	ND
Early neurological improvement	87	17 (19.5)	11.8–29.5
Early neurological deterioration	87	15 (17.2)	9.9–26.9
Access to the ICU	93	28 (30.1)	21.0–40.5
Any ICH	93	23 (24.7)	16.3–34.8
HI 1		11 (11.8)	
HI 2		6 (6.5)	
PH 1		2 (2.2)	
PH 2		4 (4.3)	
Symptomatic ICH	93	5 (5.4)	1.7–12.1
Non-neurological adverse event within 30 d			
Any non-neurological adverse event	93	25 (26.9)	18.2–37.1
Pulmonary coinfection		2 (2.2)	
Heart failure/acute myocardial infarction		5 (5.4)	
Pulmonary embolism		2 (2.2)	
Deep venous thrombosis		4 (4.3)	
Respiratory failure		7 (7.5)	
Renal failure		2 (2.2)	
Multiorgan failure and disseminated intravascular coagulation		2 (2.2)	
Endocarditis		1 (1.1)	

Values are n (%) or median (IQR) unless otherwise as indicated. First pass effect defined as mTICI 2b/3 after first pass, early neurological improvement as 24 hours NIHSS decrease ≥ 8 points or 24 h NIHSS 0–1, and early neurological deterioration as 24 hours NIHSS increase ≥ 4 points. COVID-19 indicates coronavirus disease 2019; HI, hemorrhagic infarction; ICH, intracranial hemorrhage; ICU, intensive care unit; IQR, interquartile range; mTICI, modified Thrombolysis in Cerebral Infarction; ND, Not done; NIHSS, National Institutes of Health Stroke Score; and PH, parenchymal hematoma.

* Data among patients with clot retrieval (excluding 4 cases with recanalization after intravenous thrombolysis and 1 case with attempted catheterization).

† Data among patients with successful reperfusion.

Table 3. Comparison of Biological Data Assessed Within 48 Hours of Admission Between Patients Alive and Dead at 30 Days

Biological parameters	30-day mortality		P value
	No (n=66)	Yes (n=27)	
Red blood cell count, $10^{12}/L$	4.5±0.6	4.2±0.8	0.051
White blood cell count, $10^9/L$	8.9 (6.7–12.5)	9.7 (7.1–11.9)	0.41
Platelet count, $10^9 /L$	278±110	281±127	0.89
Hemoglobin, g/dL	13.1±1.4	12.4±1.8	0.064
Hematocrit, %	39.4±4.6	37.1±6.0	0.068
Neutrophil count, $/mm^3$	6705 (4850–9200)	7765 (5280–9160)	0.55
Lymphocyte count, $/mm^3$	1325 (930–2000)	900 (605–1325)	0.004
Potassium, mmol/L	4.0±0.5	4.0±0.4	0.88
Sodium, mmol/L	140±3.9	138±3.5	0.10
Creatinine, $\mu mol/L$	72 (62–92)	77 (56–116)	0.26
Alanine, IU/L	26 (17–51)	42 (35–50)	0.42
Aspartate, IU/L	26 (20–37)	52 (32–55)	0.003
High-sensitivity C-reactive protein, mg/L	12.6 (2.9–38.5)	21.9 (7.7–40.0)	0.24
Lactate dehydrogenase, IU/L	271 (207–399)	503 (376–787)	<0.001
D-dimer, ng/mL	2177 (853–5250)	4242 (1060–13 010)	0.24
Fibrinogen, g/L	4.0±2.2	4.2±2.0	0.73
Prothrombin time, s	13.4±2.0	14.3±2.4	0.26
Activated partial thromboplastin time s	31.0±5.7	29.5±3.6	0.42

Values are median (interquartile range) or mean±SD.

Figure. **Flow chart of patient inclusion in the European ET-COVID study (Endovascular Thrombectomy in COVID-19 Patients).** COVID-19 indicates coronavirus disease 2019; LVO, large vessel occlusion; MT, mechanical thrombectomy; and RT-PCR, reverse transcription polymerase chain reaction.

