

# Mechanical Thrombectomy Outcomes in COVID-19 Patients With Acute Ischemic Stroke

## A Narrative Review

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**Background:** Coronavirus disease 2019 (COVID-19) has been shown to associate with increased risk of thromboembolic events. Mechanical thrombectomy (MT) has long been used to effectively manage those with large-vessel occlusive (LVO) stroke and has similarly been implemented in the management of stroke in COVID-19 patients.

**Review Summary:** The COVID-19 pandemic took the health care sector by a storm. Thus, less is known about MT outcomes in this population and evidence suggesting poor outcomes postthrombectomy for COVID-19 patients is accumulating. We provide a narrative on some of the published studies on the outcomes of MT in COVID-19 patients with LVO between March 2020 and February 2021. A description of patient characteristics, risk factors, COVID-19 infection severity, stroke features and thrombectomy success in this population is also presented as data from several studies show that LVO in COVID-19 patients may have some distinguishing characteristics that make management more challenging.

**Conclusions:** The effect of COVID-19 on the long-term prognosis of stroke patients after thrombectomy is yet to be determined. The accumulating evidence from current studies indicates a negative impact of COVID-19 on outcomes in acute ischemic stroke patients who receive MT, irrespective of timely, successful angiographic recanalization. This review may help alert clinicians of some of the COVID-19-specific postthrombectomy challenges.

**Key Words:** COVID-19, acute ischemic stroke, large-vessel occlusion, mechanical thrombectomy

(*The Neurologist* 2021;26:261–267)

### BACKGROUND

Coronavirus disease 2019 (COVID-19) is associated with a myriad of thromboembolic events, one of which is acute ischemic stroke (AIS).<sup>1</sup> The hypercoagulable state induced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, among other factors, has been implicated in the higher frequency of thromboembolic disorders in this population.<sup>2,3</sup> Unlike traditional risk factors of ischemic stroke in the general population, large-vessel occlusive (LVO) stroke in COVID-19 patients can occur at a young age, with absence of vascular risk factors/comorbidities and can have multi-territory vascular involvement.<sup>4,5</sup> Alarming, the case fatality rate in this subset of patients was reported at 44.2%.<sup>3</sup> One of the earlier studies on the pandemic showed that COVID-19 patients with LVO stroke have an in-hospital all-cause

mortality of 60%, compared with an overall mortality of 11% in patients without the infection. This highlights the comparatively poor outcome in this population and calls for investigating reasons accounting for this disparity.<sup>6</sup> We provide an overview of the outcomes of mechanical thrombectomy (MT) in COVID-19 patients with LVO. We also describe patient characteristics, risk factors, COVID-19 infection severity, stroke features and thrombectomy success in COVID patients with LVO stroke. The evidence presented in this review may help clinicians anticipate some of the pitfalls in the management of COVID-19 patients with LVO stroke.

### METHODS

We conducted a literature search utilizing the PubMed search engine by using different combinations of the terms: COVID, thrombectomy, stroke, LVO and outcomes. We reviewed observational cohort studies, case-control studies, case series, case reports and systematic reviews published between March 2020 and February 2021 and included articles describing COVID-19 patients with LVO stroke who underwent MT, in addition to details of their risk factors, COVID-19 severity, clinical presentation, laboratory results, angiographic results and thrombectomy outcomes. Furthermore, for the purpose of comparison, we included a few important studies describing COVID-19 stroke patients in general, regardless of having undergone MT or not. We believe that these studies help present a more complete picture.

### Review of the Literature

#### Impact of COVID-19 Pandemic on Stroke Time-to-Treatment

The COVID-19 pandemic took the health care sector by a storm. Not only did it disrupt management of chronic conditions and elective procedures, but life-saving emergency procedures, in which time is critical, have been delayed or even aborted.<sup>7,8</sup> In AIS patients, MT must be performed in a timely manner; if an MT is not performed within 6 hours of when an AIS patient was last seen in his/her normal state, it loses its benefit. In a select group of patients, those with potentially salvageable tissue identified on computed tomography perfusion or magnetic resonance imaging, that window is extended to 24 hours.<sup>9</sup>

Several reports describe delayed presentation of AIS patients because of anxiety associated with being in the hospital during the pandemic, many of whom had an extremely poor outcome.<sup>10</sup> If the patient did manage to make it to the hospital in time, the service itself during the pandemic is associated with many logistic and clinical challenges. SARS-CoV-2 is highly contagious, and the virus may spread via droplets or become aerosolized during intubation. Thus, additional precautions

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ISSN: 2331-2637/21/2606-0261

DOI: 10.1097/NRL.0000000000000360

before intubation are required such as using appropriate protective gear, using special equipment and performing manual ventilation and intubation before arrival to the angiographic interventional suite. Furthermore, the physical movement of the team members in these suites must be highly controlled to reduce the risk of transmission. In addition, strict measurements of systolic blood pressure, mean arterial pressure and end tidal carbon dioxide are needed to avoid poor outcomes such as disability and death in this population.<sup>9</sup> Overall, data from different parts of the world show that the pandemic has had a negative impact on AIS time-to-treatment metrics, a factor which plays a key role in predicting clinical outcomes in stroke patients.<sup>11,12</sup>

### Demographic Characteristics, Laboratory and Risk Factors of COVID Patients Treated With MT

Data on demographic characteristics of COVID-19 patients treated with MT indicate a wide range of age groups. While some studies reported on young patients in their thirties with an obvious male predominance,<sup>5,10</sup> other studies reported a high frequency of MT in older male COVID-19 patients with a median age of more than 70 years.<sup>13–15</sup> Overall, according to a meta-analysis of 50 studies, COVID-19 patients with acute cerebrovascular disease were found to be younger than stroke patients with no SARS-CoV-2 infection (pooled median difference = 6.0 y).<sup>16</sup> In a parallel manner, COVID-19 patients who underwent mechanical thrombectomy were younger than uninfected patients who underwent MT during both the pandemic<sup>6</sup> and before the pandemic (Table 1).<sup>17</sup> Interestingly, in addition to being younger, some studies on MT reported many COVID-19 patients with AIS lacking traditional vascular risk factors,<sup>5,10</sup> although many other studies described the presence of these risk factors (eg, hypertension, diabetes and cardiovascular disease) in COVID-19 patients treated with MT.<sup>6,13–15</sup>

Data from several studies describe distinguishing laboratory findings in COVID-19 patients with AIS, such as elevated levels of D-dimer, ferritin, lactate dehydrogenase (LDH), lupus anticoagulant, anticardiolipin immunoglobulin A, and antiphospholipid immunoglobulins.<sup>3,27,28</sup> This was consistent with studies on COVID-19 patients who underwent MT (Table 1).<sup>10,13,17,18</sup> Importantly, specific laboratory findings in COVID-19 patients may have diagnostic, prognostic, and possible therapeutic implications.<sup>13,29–32</sup> An example of the prognostic value of such data is from studies on COVID-19 pneumonia patients which suggest that high levels of D-dimer, interleukin-6, LDH, and ferritin on admission, along with abnormal coagulation values—all of which were frequently found in COVID-19 patients who underwent MT<sup>10,13,17,18</sup>—are associated with a higher mortality risk.<sup>30,31</sup> In addition, laboratory indicators such as low lymphocyte count and high aspartate and LDH levels were significantly associated with 30-day mortality after MT in COVID-19 patients and can be used as predictors of mortality in these patients.<sup>13</sup> The proposed therapeutic benefit of these laboratory values lies in possibly guiding clinicians to the appropriate anticoagulation dose in COVID patients, whether be it for prophylaxis or for patients undergoing MT. In case of prophylaxis, many reports showed a high frequency of cerebrovascular disease in COVID-19 patients despite receiving a standard prophylactic regimen.<sup>1,6,32</sup> Some investigators further suggest that standard low molecular weight heparin may be insufficient and higher doses of prophylaxis may be required in COVID-19 patients with a high risk for cerebrovascular disease and markedly elevated laboratory coagulopathy indicators.<sup>1,32</sup> Nevertheless, in patients

with COVID-19-related critical illness who do not have suspected or confirmed venous thromboembolism, the American Society of Hematology still recommends using prophylactic-intensity over intermediate-intensity or therapeutic-intensity anticoagulation.<sup>33</sup> In patients undergoing thrombectomy, it may be prudent to monitor inflammatory markers as it has been suggested that those with elevated markers may require aggressive anticoagulation and prolonged observation at the peak of their immune response.<sup>26</sup>

### COVID-19 Severity at the Time of Stroke in MT Patients

Severe SARS-CoV-2 infection has been shown to associate with increased mortality risk in stroke patients who were treated with MT (Table 1). Data from multiple studies suggests that MT in COVID-19 patients with stroke is in fact successful, but the severity of the underlying pneumonia may affect the overall outcomes.<sup>4,13,14</sup> Thrombectomy in severe infection is complicated by diagnostic and therapeutic delays imposed by the fact that these patients are more likely to be sedated and intubated, thus hindering the early detection of any deterioration in the level of consciousness. Other challenges in this population include multiorgan damage, complicated patient management pathways, COVID-19-associated arterial disease and hypercoagulability.<sup>4</sup> A study from Spain concluded that COVID-19 was an independent predictor of in-hospital mortality. The same group also found that despite receiving MT, LVO in COVID-19 patients was associated with 50% in-hospital mortality and most of the patients who died (80%) had a severe SARS-CoV-2 infection.<sup>14</sup> A multicenter cohort study involving 34 European stroke centers studied COVID-19 patients with LVO who underwent MT and showed that 27% of their patients experienced non-neurological complications and close to one third of them required intensive care unit management. They concluded that, generally, the risk of mortality in this subset of patients depends on the severity of the infection, patient comorbidities, age, and laboratory abnormalities.<sup>13</sup>

Of note, studies on COVID-19 patients with MT showed that stroke can be the first manifestation of SARS-CoV-2 infection.<sup>10,15,19,20</sup> Therefore, clinicians must suspect COVID-19 diagnosis in stroke patients who present to the hospital with altered levels of consciousness, especially during the pandemic time. That level of suspicion must also be maintained when dealing with confusion or even unconsciousness in diagnosed COVID-19 patients because though it could be related to the severity of their underlying infection, it may also be a sign of stroke.<sup>34</sup>

### Stroke Characteristics in COVID-19 Patients Treated With MT

Evidence supports a higher frequency of cryptogenic stroke in COVID-19 patients.<sup>3</sup> In a study from New York, 65.6% of stroke cases in COVID-19 patients were cryptogenic; a rate much higher than that documented in contemporary uninfected (30.4%) and historical controls (25.0%).<sup>18</sup> In general, studies showed that stroke patients with COVID-19 were more impaired on presentation with higher National Institutes of Health Stroke Scale (NIHSS) scores on admission than contemporary<sup>18</sup> and historical controls.<sup>16,35</sup> Similarly, on presentation, higher NIHSS scores were seen in COVID-19 patients who underwent MT (Table 1).<sup>5,6,17,23</sup>

Other notable stroke features in COVID-19 patients who were treated with MT include a higher frequency of LVO, higher thrombus burden with a tendency for clot fragmentation, multiterritory vascular involvement and uncommon stroke

**TABLE 1.** Clinical, Laboratory, Thrombectomy Success and Outcomes in COVID-19 Patients With Stroke Who Underwent Mechanical Thrombectomy

References	MT Patient Characteristics [n (%)]	COVID Severity in MT Patients [n (%)]	Laboratories in MT Patients [n (%)]	Thrombectomy Success [n (%)]	Outcomes [n (%)]
John et al <sup>5</sup>	n = 6 Age average 46.8 5 (83.3) males 1 (16.6) HTN, DM 5 (83.3) no risk factors NIHSS 23	3 (50) no symptoms 3 (50) fever, cough, dyspnea	—	3 (50) TICI 3 1 (16.6) TICI 2b 1 (16.6) TICI 2a 1 (16.6) TICI 0	1 (16.6) mRS 1 1 (16.6) mRS 3 4 (66.7) mRS 4-5 (at discharge or 30 d poststroke)
Escalard et al <sup>6</sup>	n = 10 Age median 59.5 8 (80) males 8 (80): ≥ 1 stroke risk factor NIHSS average 22	2 (20) no symptoms 5 (50) mild symptoms 3 (30) Hospitalized for COVID	—	9 (90) successful recanalization (TICI ≥ 2b) 4 (40) reocclusion within 24 h	6 (60) In-hospital death
Oxley et al <sup>10</sup>	n = 4, Age range (37-49) 4 (100) males 1 (25) Hx of stroke NIHSS average 16	2 (50) no symptoms 1 (25) lethargy 1 (25) fever, cough, lethargy	3 D-dimer 1000+ 2 (50) Fibrinogen 500+ PT/PTT normal	—	1 (25) Home 1 (25) rehabilitation 2 (50) Hospitalized (ICU) NIHSS average 10
Cagnazzo et al <sup>13</sup>	n = 93 Age median 71 63 (67.7) males 43 (46.2) Cardiovascular disease NIHSS median 17	32 (34.4) no symptoms 31 (33.3) fever 31 (33.3) dyspnea	D-dimer median 2440 CRP 15.4 (4-40) PT/PTT normal	74 (79.6) Successful recanalization (TICI 2b-3) 2 (2.2) reocclusion of the same artery	27 (29) 30-day mortality Cause of mortality: 14 (15.1) neurological 13 (14) Non-neurological NIHSS at 24 h (median) 14
Requena et al <sup>14</sup>	n = 10 Age average 70.8 6 (60) males 2 (20) Atrial fibrillation NIHSS median 18	9 (90) Prestroke symptoms 2 (20) ICU admission 7 (70) Severe infection	—	5 (50) TICI 2b-3	NIHSS at 24 h (median) 18 5 (50) In-hospital death
Pop et al <sup>15</sup>	n = 13 Age median 78 5 (38.4) males NIHSS median 13	12 (92.3) patients presented to the hospital for stroke 4 (33.3) prestroke symptoms	—	10 (76.9) TICI 2b-3 1 (7.6) reocclusion within 9 h	NIHSS median 5 (last available) 2 (15.3) In-hospital death
Yaghi et al <sup>18</sup>	n = 6 Age average 55 6 (100) comorbidities 2 (33) Atrial fibrillation	1 (16.7) no symptoms 1 (16.7) cough only 4 (66.7) hypoxia	All with ↑ D-dimer ↑ CRP 5(83) D-dimer 2700+	—	2 (33) rehabilitation 2 (33) Hospitalized (ICU) 2 (33) In-hospital death 1 (20) Home NIHSS 1
Wang et al <sup>17</sup>	n = 5 Age average 52.8 4 (80) males 4 (80) comorbidities NIHSS average 23	—	All with ↑ D-dimer ↑ ESR, CRP ↑ INR, ↑ PTT ↑ interleukin-6	1 (20) TICI 3 2 (40) TICI 2b 2 (40) TICI 2a 2 (40) reocclusion within minutes	Full recanalization 3 (60) In-hospital death Hemorrhagic conversion 10 d after discharge
Al Saiegh et al <sup>19</sup>	n = 1 Age 62, female No risk factors	Patient presented to the hospital for stroke	—	Full recanalization	Hemorrhagic conversion 10 d after discharge
Grewal et al <sup>20</sup>	n = 3 Age average 47.5 NIHSS average 16	1 (33.3) COVID symptoms 2 (66.7) patients presented to the hospital for stroke	D-dimer 1 (33.3) normal 2 (66.7) 15,000+	1 (33.3) TICI 3 2 (66.7) TICI 2b	2 (66.7) rehabilitation mRS 4 1 (33.3) In-hospital death
Yaeger et al <sup>21</sup>	n = 10 5 (50) COVID positive 5 (50) COVID negative NIHSS average 14 NIHSS range: 10-19	n = 5 5 (100) no fever, no critical respiratory illness 3 (60) cough, dyspnea	—	n = 10 9 (90) successful recanalization (TICI ≥ 2b)	NIHSS score was reduced by an average of 7.7 points
De Havenon et al <sup>22</sup>	n = 104 average ≤ 50: 25 (24) 71 (68.3) males 30 (28.9) Atrial fibrillation	56 (53.9) Mechanical ventilation	—	—	49 (47.1) Favorable discharge 31 (29.8) In-hospital death
Al Kasab et al <sup>23</sup>	n = 13 Age median 58 8 (61.5) males NIHSS median 19	—	—	13 (100) Successful recanalization (TICI ≥ 2b)	mRS on discharge (median) 4 (3-6) 2 (16.7) mRS (0-2) 4 (33.3) In-hospital death

TABLE 1. (continued)

References	MT Patient Characteristics [n (%)]	COVID Severity in MT Patients [n (%)]	Laboratories in MT Patients [n (%)]	Thrombectomy Success [n (%)]	Outcomes [n (%)]
Mansour et al <sup>24</sup>	n = 1 Age 54, Female No risk factors NIHSS 11	Used to be isolated in isolation hospital/institution	D-dimer 490 µg/L CRP 21	Successful recanalization (TICI 3)	NIHSS 2 after extubation
Pisano et al <sup>25</sup>	n = 1 Age 33, female Morbid Obesity NIHSS 15	Cough, fever, lethargy	D-dimer 90,000+ Anticardiolipin IgM mildly elevated	Unsuccessful recanalization (TICI 2a)	Malignant cerebral edema In-hospital death
Sweid et al <sup>26</sup>	n = 15 Age average 64.6 8 (53) males NIHSS 15	—	—	15 (100) Successful recanalization (TICI 2b/3)	5 (33.3) death

National Institutes of Health Stroke Scale (NIHSS) scores range from 0 to 42, with higher numbers indicating more severe stroke; modified Rankin Scale (mRS) scores range from 0 to 6, with higher numbers indicating more severe disability; thrombolysis in cerebral infarction (TICI) scores range from 0 to 3, with 3 indicating complete perfusion. Laboratory reference ranges are as follows: fibrinogen: 175 to 450/mg/dL; D-dimer: 0 to 500 ng/mL.

COVID-19 indicates coronavirus disease 2019; CRP, C-reactive protein; DM, diabetes mellitus; ESR, erythrocyte sedimentation rate; HTN, hypertension; Hx, history; ICU, intensive care unit; INR, international normalised ratio; MT, mechanical thrombectomy; PT, prothrombin time; PTT, partial thromboplastin time.

locations, all of which are associated with increased mortality risk.<sup>5,10,17,36</sup> Clinicians should pay attention to the above mentioned radiologic characteristics and when present, a concomitant SARS-CoV-2 infection in patients with AIS must be suspected, especially in the days of the pandemic and in those with no vascular risk factors.<sup>35</sup> Neuroimaging studies of COVID-19 patients also showed that ischemic strokes were unexpectedly frequent (35.3%) in the vertebrobasilar territory.<sup>37</sup> Moreover, although the cause of stroke is often cryptogenic, other ischemic stroke subtypes were also encountered in COVID-19 patients such as LVO, cardiogenic embolism and arterial dissection.<sup>18,26,37,38</sup>

### MT Success in COVID-19 Patients

On the basis of appropriate imaging and after identifying potentially salvageable tissue, current guidelines recommend MT in patients who present with AIS symptoms caused by occlusion of the intracranial internal carotid artery or proximal middle cerebral artery up to 24 hours of last known normal.<sup>39</sup> It is clear, however, that reperfusion procedures during the pandemic face several challenges. An early pandemic case series of 5 COVID-19 patients from New York presented many of the technical challenges encountered in these patients when undergoing MT<sup>17</sup>; the intravascular clots in these patients were characterized by high fragility, extensive clot burden and were especially vulnerable to fragmentation and distal downstream migration as well as translocation to new vascular territories.<sup>17</sup> These patients were more likely to have worse radiographic and clinical outcomes post-MT. This is consistent with another study in France where they performed MT in COVID-19 patients and noticed a high clot burden in multiple arterial irrigation zones, absence of first-pass effect, and a tendency for early postthrombectomy arterial reocclusion.<sup>6</sup> A pooled analysis of LVO in 39 COVID-19 patients who underwent MT showed that 89.7% were found to have a high NIHSS score at admission (19.0) and on average, 1.5 involved vessels and 2.3 attempts (passes) to retrieve the clot. Importantly, although 77% of the MT patients achieved a successful reperfusion with thrombolysis in cerebral infarction score of 2B/3, the mortality rate was extremely high (45.9%).<sup>26</sup> It is worth noting that while reviewing the literature, we noticed that multiple studies reported very poor outcomes in spite of achieving successful reperfusion with MT (Table 1).<sup>5,6,13,14,19,23,26</sup>

The hypercoagulability associated with COVID-19 poses extra challenges for the interventional radiologists to overcome. Maneuvers usually performed during LVO treatment in disseminated intravascular coagulation, cancer-associated coagulopathy, and sepsis may be needed such as administration of intraluminal fibrinolytics or antiplatelet agents, conducting multiple passes to retrieve a clot, using aspiration devices and stent deployment.<sup>4</sup>

### Outcomes of MT in COVID-19 Patients

Evidence from multiple published studies supports an association between COVID-19 and longer hospital stay, higher complications rates, worse functional outcomes and higher in-hospital mortality rates in AIS/LVO patients—whether they underwent MT or not—when compared with those without the infection.<sup>3,16–18,26,35,40,41</sup> A comprehensive cross-sectional study of patients from a large New York-based health care system found that stroke patients with COVID-19 had over a 9-fold increase in mortality compared with those without the infection.<sup>42</sup> Interestingly, they identified a higher risk of unfavorable outcomes in COVID-19 patients with ischemic stroke independent of traditional stroke risk factors and surrogates of stroke severity, which they attributed to the respiratory impact of COVID-19 on an already compromised patient with stroke.<sup>42</sup> Reviewing the published literature on MT outcomes in COVID-19 patients, findings were similar to the aforementioned studies, with a few exceptions. The vast majority of studies showed that LVO patients who underwent MT and had a concomitant SARS-CoV-2 infection had a high mortality rate, despite timely intervention and successful reperfusion (Table 1).<sup>5,6,13,14,19,23,26</sup> Moreover, MT in this subset of patients called for complex maneuvers due to multiple territory involvement, both arterial and venous vasculature involvement, unfavorable clot consistency and high clot burden.<sup>26</sup> In addition to the high in-hospital mortality (50%) seen in this population, patients who survived, were more likely to suffer poor functional outcomes and had higher NIHSS scores (a median of 18.0) 24 hours postthrombectomy.<sup>14</sup> In contrast to the majority of studies supporting worse outcomes in COVID-19 patients who underwent MT for LVO, a prospective study from 28 thrombectomy-capable stroke centers in North America, South America, and Europe showed that COVID-19 patients who underwent MT for LVO had similar in-hospital mortality rate,

duration of hospitalization, discharge modified Rankin Scale scores and rate of functional independence (modified Rankin Scale 0 to 2) at discharge as non-COVID-19 patients.<sup>23</sup>

The poor outcomes reported in AIS patients with COVID-19 postthrombectomy led a group of investigators to compare this population to AIS patients with COVID-19 who did not undergo thrombectomy. This study found that COVID-19 patients who underwent thrombectomy (who comprised 3.3% of the 3165 patients treated with MT), had a near identical rate of death to COVID-19 patients with AIS who did not undergo thrombectomy (note that patients with lacunar stroke or non-occlusive atherosclerotic stroke do not receive MT).<sup>43,44</sup> This suggests that the higher rates of poor outcome were inherent to SARS-CoV-2 infection. Interestingly, when both of these groups were compared, MT patients had a higher rate of favorable discharge than those who did not undergo the procedure.<sup>22</sup> Given the improved outcomes following reperfusion, eligible COVID-19 patients with AIS should undergo MT.<sup>22,45,46</sup> It is worth noting that the same group reported that COVID-19 was a significant predictor of mortality despite adjusting for comorbidities such as respiratory failure, acute renal failure, and duration of hospitalization.<sup>22</sup>

Postthrombectomy care is an important aspect of LVO management. Hemorrhagic transformation of ischemic infarcts has been reported in COVID-19 stroke patients, including patients who underwent MT.<sup>13,19,26,47,48</sup> In a study that included 11 hospitals in New York, they reported 72 AIS patients with SARS-CoV-2 infection, 20.8% of whom had associated brain hemorrhage, including 6 patients with hemorrhagic transformation and 9 patients with simultaneous hemorrhage and infarction.<sup>48</sup> Similar rates were reported postthrombectomy in a study on 93 COVID-19 patients, with the rate of intracranial hemorrhage reported to be 24.7% (23 patients) and the rate of symptomatic intracranial hemorrhage being 5.4% (5 patients).<sup>13</sup> It has been suggested that SARS-CoV-2 infection may increase the risk of hemorrhagic stroke,<sup>49</sup> however, it is not known whether some of the documented intracranial hemorrhage cases in COVID-19 patients with AIS are the result of the infection and its associated cytokine storm or a consequence of anticoagulation.<sup>47,50</sup> Another postthrombectomy complication is early arterial reocclusion,<sup>6,13,15,17</sup> which was documented in up to 40% of the patients who received MT in some case series.<sup>6,17</sup> It was suggested that reocclusion was a sequela of the procoagulant state associated with SARS-CoV-2 infection. Moreover, the risk of recurrent strokes was found to be higher in AIS patients with COVID-19. One of the reports on ischemic stroke in COVID-19 patients documented a recurrence rate of 10% during the same admission.<sup>51</sup> This is considerably high compared with a historical in-hospital stroke recurrence of only 0.8%.<sup>52</sup> Therefore, continuous monitoring and frequent evaluation following MT is warranted to promptly diagnose and treat any of the frequently encountered complications in this population, all the while adhering to infection control protocols (Table 1).

## DISCUSSION

The poor clinical outcome of MT in COVID-19 patients with AIS is documented in the literature and is attributed to a combination of patient risk factors and the underlying COVID-19 pathology. Multiple cohort studies suggest that the severity of the underlying pneumonia may affect overall outcomes<sup>4,13,14,22</sup>; COVID-19 patients are sicker and have more systemic complications than patients without COVID-19.<sup>22</sup> This is believed to account for the worse reperfusion outcomes. Of the documented COVID-19 complications that may be of

relevance, acute respiratory failure, acute renal failure, and coagulopathy were the most frequently encountered.<sup>53</sup> A multicenter cohort study found that the poor prognosis postthrombectomy in COVID-19 patients with stroke was not explained by the traditional predictors of poor outcomes in stroke patients such as NIHSS scores but was likely determined by the severity of the underlying infection, patient comorbidities, age, and laboratory indicators such as low lymphocyte count and high aspartate and LDH levels. These laboratory findings were significantly associated with 30-day mortality after MT in COVID-19 patients and can therefore be used as mortality predictors in this population.<sup>13</sup>

Despite achieving successful recanalization with MT, several investigators reported poor outcomes in COVID-19 patients.<sup>5,6,13,14,19,23,26</sup> This can be attributed to higher rates of both neurological and non-neurological complications. Significant non-neurological complications such as respiratory and cardiac failure, deep venous thrombosis/pulmonary embolism, pneumonia and multiorgan failure were responsible for the poor prognosis and in part, for the high mortality rates seen in COVID-19 postthrombectomy. Neurological complications such as intracranial hemorrhage and malignant cerebral infarction or edema were the main causes for morbidity and mortality in COVID-19 patients after MT.<sup>13</sup> It is widely believed that the underlying systemic inflammation, accompanied by respiratory complications with subsequent cerebral oxygenation and hemodynamic alterations may play an important role in the poor outcomes seen postthrombectomy in those with SARS-CoV-2 infection.<sup>5,13</sup> Interestingly, COVID-19 associated endotheliitis and intravascular neutrophil extracellular traps were proposed by Escalard et al<sup>6</sup> to explain why despite recanalization, patients were still unable to achieve successful reperfusion; in spite of a successful clot removal via thrombectomy, the diffuse microvascular thromboinflammation injury/endotheliitis seen in COVID patients result in a compromised systemic microcirculatory function in multiple vascular beds and organs. In addition, the vascular inflammation in COVID-19 patients is associated with a diffuse microangiopathy which accounts for the increased risk of recurrent thrombosis/stroke and early reocclusion seen in this population following MT. The other proposed theory involves the formation of intravascular neutrophil extracellular traps, structures that have been shown to play a key role in initiating both arterial and venous thrombosis, ultimately leading to organ damage and high mortality rate in COVID-19 patients.<sup>6,54–56</sup> In light of the aforementioned findings, we believe attention must be diverted towards therapies that target the inflammatory drivers of SARS-CoV-2 infection to reduce its severity once established and improve the high mortality rates reported in this population.

The limitations of this review include the following: it is a narrative review aimed at summarizing the available published literature on the outcomes of thrombectomy in COVID-19 patients with LVO, which is a relatively new diagnostic challenge with many unknown attributes. In addition, this review carries the inherent defects of the studies included in which key information pertaining to patients' risk factors, stroke severity, infection severity, laboratories and long-term outcomes may have been overlooked. Moreover, these studies adopted different approaches and were conducted on different populations with distinct features and are hence expected to carry some heterogeneity in terms of findings. Finally, given that most of the available studies were written while the patients were still hospitalized or recently discharged to rehabilitation facilities, we were not able to report on the long-term outcomes of COVID-19 patients who received thrombectomy.

## CONCLUSIONS

The effect of COVID-19 on the long-term prognosis of stroke patients after thrombectomy is yet to be determined. The accumulating evidence from current studies indicates a negative impact of COVID-19 on outcomes in AIS patients who receive MT, irrespective of timely, successful angiographic recanalization. Patients with SARS-CoV-2 infection suffer longer hospital stays, more complications, worse clinical outcomes, and higher mortality rates compared with those without the infection. This can be attributed to a combination of patient risk factors and the effects of the underlying COVID-19 pathology. Clinicians should be on the lookout for complications such as early reocclusion, hemorrhagic conversion and recurrent strokes postreperfusion. Therefore, continuous monitoring and frequent evaluation postthrombectomy are crucial. Moreover, adherence to infection control protocols and prompt detection of any neurological deterioration is equally important. Finally, MT amidst a pandemic calls for some modifications with some groups having already published recommendations for specifically managing COVID-19 patients undergoing MT.<sup>9,57-60</sup>

This review may help clinicians anticipate some of the pitfalls imposed by the SARS-CoV-2 infection on the management and prognosis of stroke patients after thrombectomy. It also emphasizes the need for therapies that target the inflammatory drivers of COVID-19 to decrease the high disability and mortality rates seen in this population.

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