Endovascular Thrombectomy of COVID-19-Related Large Vessel Occlusion: A Systematic Review and Summary of the Literature

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Abstract

Purpose Despite an overall reduction in the number of stroke cases presenting to hospitals during the COVID-19 pandemic, a remarkably high incidence of acute cerebrovascular disease associated with the infection has been reported. In this systematic review, we assess the neurological outcomes and complications of endovascular thrombectomy (EVT) for large vessel occlusions (LVO) in COVID-19 patients.

Methods A literature search was performed in PubMed from December 1, 2019 through September 1st, 2020 using different combinations of suitable keywords. Ten studies reporting EVT outcomes and complications were identified. Two studies that included non-LVO pathologies and COVID-19 negative patients with the outcomes analysis were excluded. Patient demographics, comorbidities, anatomic thrombus location, neurological and angiographic outcomes were assessed.

Results A total of 8 studies, in addition to our institutional case series, were ultimately included in this review. The mean age was 62.2 years, of which 67.6% were males. M1 segment involvement was the most commonly reported (53.8%) thrombus location. The mean NIHSS at presentation was 20.4 with no significant change at 24 h. Successful revascularization (TICI ≥ 2b) was achieved in 89%. Early proximal cerebral re-occlusion was reported in 6 patients (11%) and cerebral hemorrhage in 3 patients (4%). In hospital mortality was reported in 15 patients (28.8%).

Conclusion Despite angiographically successful EVT of LVOs in the majority of patients, this literature analysis demonstrates overall poor outcomes and high mortality in COVID-19 patients post EVT. An unusual incidence of early intracerebral proximal arterial re-occlusion was notable.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is a new strain of the coronavirus family that emerged in 2019 and was first reported in Wuhan, China, but spread exponentially to become a worldwide pandemic in months. Infection with SARS-Cov-2 primarily presents as a severe acute respiratory illness in human subjects [1].

Understanding of the 2019-coronavirus disease (COVID-19) has evolved significantly over time. In addition to respiratory symptoms, COVID-19 may present with various gastrointestinal, renal, neurological and cardiovascular symptoms [2, 3]. Attention has been drawn recently to the thromboembolic sequelae of this disease, including ischemic strokes, due to the severe outcomes associated with these complication [4–6]. Despite a significant overall reduction in the number of stroke cases presenting to hospitals during the pandemic, studies have

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demonstrated a remarkably high incidence of acute cerebrovascular disease in those with COVID-19 [7–9].

Although the indications for endovascular thrombectomy (EVT) of COVID-19 related large vessel occlusions (LVOs) are the same as for the general population, a protected code stroke algorithm has been introduced to expedite management while also ensuring the safety of healthcare providers [10–12]. In this study, we employed meta-analytic techniques to pool data from the literature to explore the outcomes and potential complications of EVT among COVID-19 patients.

Methods

Institutional Case Series Study Design

Institutional review board approval was obtained for a retrospective study of COVID-19 positive patients with large vessel occlusions (LVO) who underwent endovascular intervention between March 1 and June 20. Informed consent was waived. We studied patients' demographics, clinical presentations, laboratory findings, National Institutes of Health Stroke Scale (NIHSS), CT angiography (CTA) and CT perfusion (CTP) findings, mechanical thrombectomy procedure, immediate post-procedural outcome and neurological outcome at final follow-up whenever available.
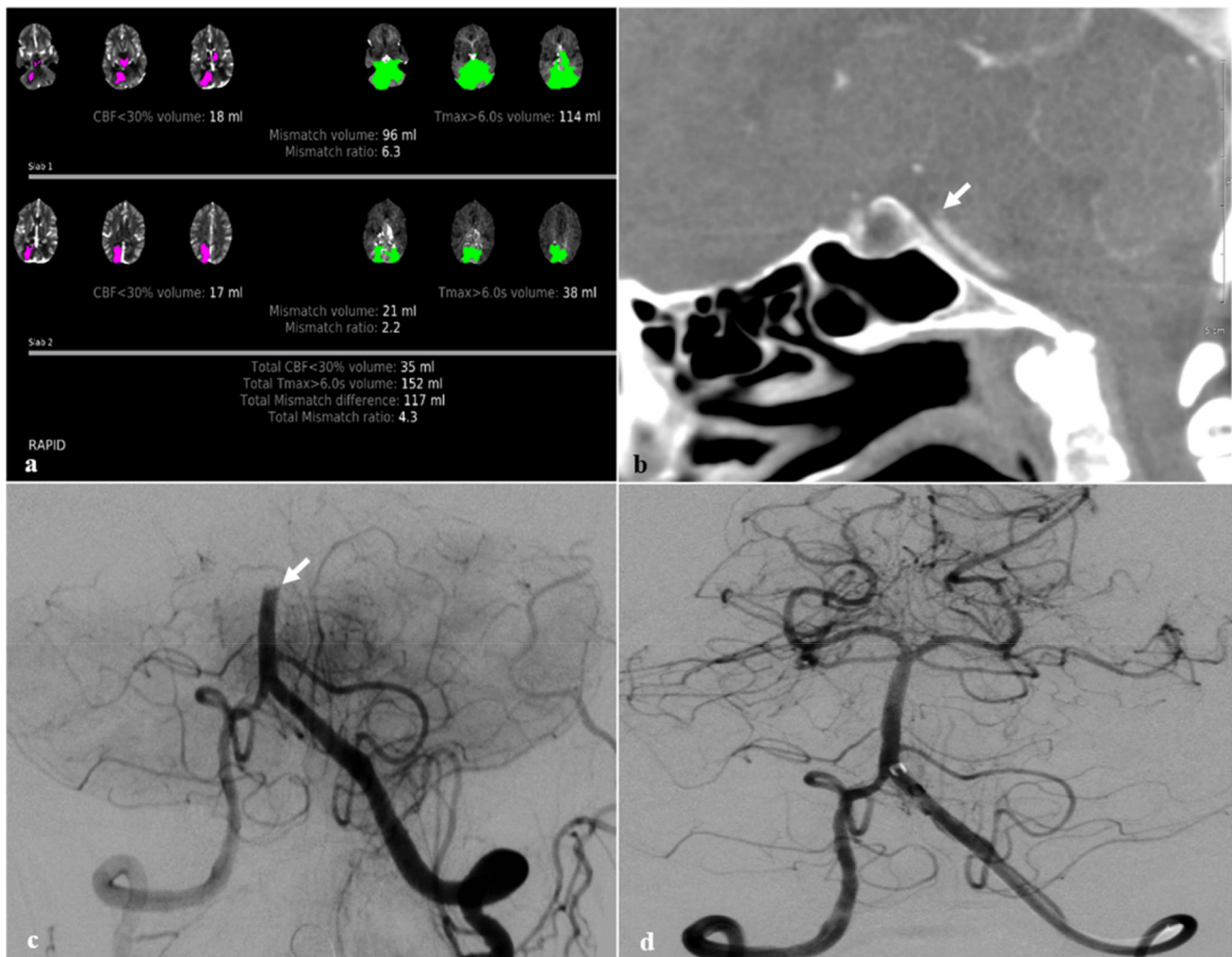

Fig. 1 A 75-year-old female with multiple comorbidities; **a** CT perfusion demonstrates a core infarction of 35 ml and mismatch ration of 4.3. **b** CTA shows occlusion of the distal basilar artery (arrow). **c** Left vertebral angiogram again reveals basilar artery occlusion. **d** Post thrombectomy angiogram reveals TICI3 perfusion

Table 1 Patient demographics, clinical presentations, laboratory work-up, endovascular and clinical outcomes

Characteristics	Patient 1	Patient 2	Patient 3
Demographics	75	71	47
Age			
Gender	F	F	F
Comorbidities			
	HTN, HLD with left carotid endarterectomy 2020, new A-fib with RVR	HTN, CAD s/p CABG 2012, HFrEF, asthma, DM type II	None
Symptoms/presentation			
COVID related symptoms before presentation	Intermittent chest tightness, dyspnea on exertion, dizziness	None	Cough, shortness of breath
Interval between onset of COVID symptoms and stroke onset	1 week	Not applicable	4 days
Symptoms on presentation	Syncope, loss of consciousness 15 h after initial presentation	Left sided weakness and left facial droop, altered mental status	Right sided weakness, left gaze deviation, loss of consciousness
Respiratory status during hospitalization	Acute hypoxemic respiratory failure secondary to COVID-19 pneumonia requiring intubation	Severe respiratory distress secondary to COVID-19 pneumonia shortly after hospitalization requiring intubation	Acute hypoxemic respiratory failure secondary to COVID-19 pneumonia requiring intubation
Initial management			
Symptoms to door time	Unknown	Unknown	40 min
tPA	Ineligible	Ineligible	Yes
Door to treatment time	15 h	80 min	159 min
Laboratory findings			
PT/INR	10.7/1.03	11.8/1.14	10.9/1.05
APTT	29	26.5	21.8
D-dimer(normal < 0.50 mg/L)	8.21	16.77	2.47
C-reactive protein (normal < 5 mg/L)		95	52.9
Interleukin-6 (normal < 6)			8
LDH (140–271 U/L)		325	
Ferritin (11–306.8 ng/ml)		98.1	10.4
Troponin I (range 3–17 ng/L)	23	25	
Antithrombin III activity (78–130)		92%	
Fibrinogen (186–466 mg/dL)		600	
Von-willebrand antigen (60–153)		> 300%	
Cardiolipin IgM (normal < 15)		20.30%	
Stroke scale rating			
NIHSS at onset	40	12	17
Imaging findings			
CTA findings	Occlusion distal basilar artery	Occlusion of right inferior M2 and paucity of the branches distally	Occlusion of distal M1 segment of left MCA
CT perfusion findings	35 ml Core infarct in the right PCA territory	58 ml Core infarct in right MCA territory	37 ml Core infarct in left MCA territory

Table 1 continued

Characteristics	Patient 1	Patient 2	Patient 3
Intervention and outcome			
Mechanical thrombectomy procedure and outcome	TICI3	TICI2b	TICI2b
Clinical outcome	Death d/t cardiac arrest from hypoxemic respiratory failure secondary to COVID-19 pneumonia	Persistent neurological deficit of left neglect and left hemiparesis	Persistent aphasia, weakness, apraxia and imbalance, dysphagia requiring PEG for feeding
Score on mRS scale at final follow-up	6	4	5

ER emergency room, *HTN* hypertension, *HLD* hyperlipidemia, *A-Fib* atrial fibrillation, *RVR* rapid ventricular response, *CAD* coronary artery disease, *CABG* coronary artery bypass grafting, *HFrEF* Heart failure with reduced ejection fraction, *DM* diabetes mellitus, *tPA* tissue plasminogen activator, *PT* prothrombin time, *INR* international normalized ratio, *APTT* activated partial thromboplastin time, *LDH* lactate dehydrogenase, *MCA* middle cerebral artery, *PEG* percutaneous endoscopic gastrostomy, *mRS* Modified Rankin Scale, *NIHSS* National Institute of Health Stroke Scale

Literature Search

We performed a literature research using the PubMed search engine on September 1st, 2020 using different combinations of the keywords COVID-19, SARS-CoV-2, stroke, large vessel occlusion and thrombectomy. Case series and treatment arms of observational studies were included. Studies that included COVID-19 negative patients and non-LVO pathologies were excluded. Patient's demographics, comorbidities, anatomic thrombus location, NIHSS at presentation and at 24 h, angiographic outcome via the thrombolysis in cerebral infarction (TICI) scale, thrombectomy technical details, and mRS.

Results

Patient Demographics

In our series, we identified 3 patients (mean age 64.3 ± 15.1) with findings consistent with acute stroke on non-contrast head CT, followed by CTA head and CT perfusion studies (An example is demonstrated Fig. 1). All the 3 patients had a sizeable ischemic penumbra and were deemed candidates for EVT according to Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE 3) criteria [13]. Two patients had anterior circulation LVO and one patient with posterior circulation LVO. Clinical presentation, treatment and outcome are detailed in (Table 1).

A total of 635 abstracts were identified from the literature search, from which 35 were identified for detailed review. Eight studies, including our case series, consisting of 73 patients were included for final analysis (Table 2). The average age of the included patients was 62.2 years,

67.6% of whom were male. All but one study included demographic data regarding vascular comorbidities. Of these, hypertension was the most prevalent (59.7%, n = 43), followed by diabetes (30.6%, n = 22), atrial fibrillation (18.5%), and hyperlipidemia (15.4%). Six studies described the basic anatomic location of cerebral thrombus location, 65.7% (n = 48) of which involved the anterior circulation. Involvement of the M1 segment was most commonly reported (53.8%). Involvement of multiple vascular territories was noted in 34.6% of cases. Carotid involvement occurred in 19.2% of cases. The mean NIHSS at presentation was 20.4 (12–40).

Intervention

In total, 47.9% (n = 35) of patients received tPA and 89% (n = 65) underwent endovascular thrombectomy. Four studies describing 42 patients provided technical EVT details. The most utilized methods were the ADAPT technique (40.5%, n = 17) and stent-aspiration combination (33.3%, n = 14). Suction aspiration only and stent retrieval were used as primary techniques in 16.7% (n = 7) and 9.5% patients (n = 4), respectively (Table 3).

Outcomes

TICI ≥ 2b was reported in 83.1% (n = 54) of cases. The mean NIHSS at 24 h after presentation (documented in three studies) was 20 (12–25), representing no significant difference compared to NIHSS at presentation. Six patients were reported to have early cerebral re-occlusion and cerebral hemorrhage occurred in three patients during the post-procedural period. In-hospital mortality was reported in 28.8% (n = 15) of patients (Table 3).

Table 2 Pooled data: patient demographics, treatments, neurological outcomes and complications

	Wang et al. [16•]	Sierra-Hidalgo et al. [25]	Escalard et al. [20]	Escalard et al. [26]	Pop et al. [27]	Valderrama et al. [28]	Yang et al. [29]	Current case series	Total (%)
Demographics									
Patients, n	5	8	10	12	13	1	21	3	73
Mean age (years)	52.8	68.5	59.5	60.1	78	52	62.3	64.3	62.2
Male, n	–	7	8	10	5	1	15	0	46
Female, n	–	1	2	2	8	0	6	3	22
Comorbidities									
DM, n	1	3	4	5	2	–	6	1	22
HTN, n	2	5	5	5	8	–	16	2	43
HLD, n	0		3	3	3	–	0	1	10
Atrial fibrillation, n		1	1	1		–	6	1	10
Thrombus location									
Anterior circulation, n (%)	5	5	9	12	8	0	13	2	54 (74)
Posterior Circulation, n (%)	1	4	1	–	5	0	–	1	12 (30)
Multiple territories, n (%)	1	1	5	6	–	1	–	0	14 (35.9)
NIHSS									
Presentation, mean (range)	27 (10–29)	27 (16–39)	22 (19–26)	19 (18–24)	13 (7–15)	20	12	23 (12–40)	Average of 20.4 (7–40)
24 h, mean (range)	–	25 (20–42)	25 (20–42)	–	–	–	10	–	20
Treatment									
tPA, n	5	0	5	8	4	1	11	1	35 (47.9)
EVT, n	5	0	10	12	13	1	21	3	65 (89)
Angiographic outcome									
TICI $\geq$ 2b, n	3	–	9	11	10	0	18	3	54 (83.1)
Clinical outcome									
Death, n	3	4	6	5	2	0	–	1	15 (28.8)
Early cerebral re-occlusion, n	0	0	4	0	1	0	0	1	6 (8.2)
Post-procedural hemorrhage, n	0	0	0	0	0	0	3	0	3 (4.1)

Discussion

The COVID-19 pandemic has demonstrated a direct and indirect impact on the occurrence and presentation of acute cerebrovascular disease. The known associated prothrombotic state leading to arterial and venous thrombosis has contributed to stroke being the most commonly reported neurological complication [4, 6]. Using meta-analytic methodology to analyze outcomes data following EVT, our study highlights the various challenges of treating COVID-19 patients presenting with stroke.

Table 3 Summary of patient characteristics and outcomes

Demographics	Total
Patients, *n*	73
Mean age (years)	62.2
Male, *n*	46
Female, *n*	22
Comorbidities	
DM, *n*	22
HTN, *n*	43
HLD, *n*	10
Atrial fibrillation, *n*	10
Thrombus location	
Anterior circulation, *n* (%)	54 (74)
Posterior circulation, *n* (%)	12 (30)
Multiple territories, *n* (%)	14 (35.9)
NIHSS	
Presentation, mean (range)	20.4 (12–40)
24 h, mean (range)	20
Treatment	
tPA, *n* (%)	35 (47.9)
EVT, *n* (%)	65 (89%)
Angiographic outcome	
TICI ≥ 2b, *n* (%)	54 (83.1)
Clinical outcome	
mRS 6 (death), *n* (%)	15 (28.8)
Early cerebral re-occlusion, *n* (%)	6 (9.2)
Post-procedural hemorrhage, *n* (%)	3 (5.6)

Although COVID-19 related LVO has been reported in young patients less than 50 years old, the mean age of this patients' pool was 62.2 years and is comparable to the mean of 68 years in pre-pandemic reports [8, 14, 15, 16•, 17]. This review found the NIHSS at presentation among COVID-19 patients is typically moderate to severe with a mean of 20.4 (range 7–40), consistent with a recent systematic review that reported a mean of 19 [18•]. In the series of patients from our institution, the two patients with anterior circulation LVO had NIHSS of 12 and 17 comparable to large-scale EVT trials who report an NIHSS range of 14–20 (mean of 17) [17]. This contrasts to the NIHSS of 40 in the patient with basilar occlusion, which was reported in 12.5% of the overall included patient pool. Re-evaluation of the NIHSS at 24 h after presentation, which was reported in three of the eight studies, demonstrated no significant difference with the NIHSS at presentation, suggesting EVT has minimal effect in the acute phase [19, 20•].

A small but significant proportion of the patients who underwent EVT (8%) had early proximal arterial re-occlusion after a successful thrombectomy. Overall post procedure intracerebral hemorrhage was 4%, which is comparable to previous EVT trials [17]. Though successful revascularization (TICI ≥ 2b) was achieved in 83% of patients regardless of technique used, the in-hospital mortality rate was high at 28.8% compared to 15.3% among non-COVID-19 patients [17]. In our series of patients, persistent neurological deficits were noted in two patients and one patient ultimately died from stroke and COVID-19 related respiratory complications. Despite a high proportion of successful angiographic results, these relatively poor outcomes compared to non-COVID-19 stroke patients may be attributed to differences in clot composition, with an increased tendency for clot fragmentation and migration that results in microemboli as described by Wang et al. [16•]. The sequalae of such microemboli are further exacerbated by the severity of the underlying COVID-19 respiratory disease that in conjunction with stroke indicates a worse overall prognosis [6].

Recent literature has reported the incidence of stroke among COVID-19 patients to range between 1.1 and 5.7% [5, 6, 9, 21, 22]. However, as patients with multiple cardiovascular risk factors are significantly more likely to develop severe COVID-19 disease as well as acute cerebrovascular disease, the association between COVID-19 and stroke is complex [23, 24]. Future research that employ multi-institutional cohorts of larger patient populations will be required to more clearly elucidate the relationship between comorbidities and LVOs related to COVID-19.

Our results are subject to inherent limitations of the retrospective nature of case series and case reports, including significant heterogeneity of included studies. Furthermore, several of the studies included in this systematic review failed to report relevant variables such as NIHSS at 24 h and mRS, and most of these were reported on a mean basis making it difficult to evaluate the progression or outcome of each patient. Future studies with a larger cohort and more detailed long-term neurological follow-up are required.

Conclusion

This systematic literature analysis demonstrates overall poor outcomes and high mortality in COVID-19 patients presenting with stroke despite angiographically successful EVT of LVOs in the majority of patients. An unusual incidence of early intracerebral proximal arterial re-occlusion and propensity for clot fragmentation and microemboli may be significant contributing factors.

Compliance with Ethical Guidelines

Conflict of interest No conflicts of interest to declare.

Disclosure No authors have financial relationships relevant to this article to disclose.

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