Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Case Report

Management of acute ischemic stroke in patients with COVID-19 infection: Insights from an international panel

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ABSTRACT

Objective: To present guidance for clinicians caring for adult patients with acuteischemic stroke with confirmed or suspected COVID-19 infection.
Methods: The summary was prepared after review of systematic literature reviews,reference to previously published stroke guidelines, personal files, and expert opinionby members from 18 countries.
Results: The document includes practice implications for evaluation of stroke patientswith caution for stroke team members to avoid COVID-19 exposure, during clinicalevaluation and conduction of imaging and laboratory procedures with specialconsiderations of intravenous thrombolysis and mechanical thrombectomy in strokepatients with suspected or confirmed COVID-19 infection.
Results: Conclusions—The summary is expected to guide clinicians caring for adult patientswith acute ischemic stroke who are suspected of, or confirmed, with COVID-19infection.

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A corona virus (SARS-CoV-2) has infected 986,776 persons as of April 2nd, 2020 over a period of 4 months. There is a possibility that Coronavirus Disease 2019 (COVID-19) infection increases the risk of stroke similar to other respiratory tract infections [1]. Approximately 5% of hospitalized patients with COVID-19 infection suffer from stroke with over 80% of them being ischemic stroke [2]. The reported mortality is 39% in patient with stroke [2] and COVID-19 infection which is much higher than the mortality observed in patients with stroke without COVID-19 infection [3]. A detailed report by an international panel of experts regarding management of ischemic stroke in COVID -19 patients was recently published [11]. Here we wish to provide insight from the panel with direct relevence to emergency medicine health care providers.

Healthcare professionals involved in evaluation and management of acute stroke patients are at risk of acquiring COVID-19 infection from suspected or confirmed COVID-19 infected patients or those who are asymptomatic carriers or in the prodromal period, or in whom neurological deficits is the first manifestation. The magnitude of risk of COVID-19 infection transmission during acute stroke patient management is not known. The time frame required to confirm the infection based on upper respiratory specimen using reverse-transcription polymerase chain reaction test and at times need for repeat testing does not allow the information to be available to stroke team members at time of decision making. Members of stroke team must use basic principles targeting prevention of disease transmission including maintaining a 1-meter distance from patient (unless absolutely necessary) and use a combination of use of surgical mask gloves, gowns, goggles or face shield and handwashing. Whether a particulate filtering facepiece respirator such as N95 (United States), FFP2 (Europe), KN95 (China), P2 (Australia/New Zealand), K94 (Korea KMOEL), or DS (Japan) is necessary is not clear as stroke evaluation does not involve aerosol generating procedures [4]. However, such use may be regulated by country and institution specific standards and also depend upon availability and regional COVID-19 infection prevalence. The stroke team evaluating the patient should comprise the minimum number of medical professionals and preferably exclude those professionals who are at high-risk for severe COVID-19 infection. Telestroke is the most effective strategy to avoid transmission by not being in the same room or space where the stroke patient with suspected or confirmed COVID-19 infection is located. All aspects of acute stroke management can be performed via Telestroke [5]. Institutions may explore with the Ethics Committee and Institutional Review Board whether commercially available low-cost smartphone application systems can substitute in locations where Telestroke networks are not available.

The high rate of mortality in COVID-19 infected patients who have multiple organ dysfunction/failure needs to be recognized and is unlikely to be influenced from acute treatment of stroke [2]. An assessment of magnitude of organ dysfunction using validated scales such as sequential organ failure assessment score maybe helpful in delineating the overall care paradigm in acute stroke patients appropriate to the expected prognosis independent of stroke related factors. Clinical evaluation and computed tomographic (CT) scan are usually supplemented by contrast-based studies such as CT angiography and CT perfusion to identify patients who are candidates for mechanical thrombectomy. Negative carrier isolator bag for patients during imaging may ensure the safety of health care providers and concurrent pulmonary imaging can identify COVID-19 pulmonary infection (Fig. 1). COVID-19 infection and stroke both have a relatively high risk of renal insufficiency and perhaps even higher when both occur together. Contrast exposure can precipitate acute kidney injury particularly in those with existing renal impairment which may subsequently increase the risk of death. Therefore, studies using contrast may be considered after evaluation of renal function and whether mechanical thrombectomy is even a consideration. There is limited data regarding use of intravenous (IV) thrombolysis in settings of infection [6]. Current guidelines do not support use of IV thrombolysis in patients with acute ischemic stroke and symptoms consistent with infective endocarditis because of the increased risk of intracranial hemorrhage [7]. However, in COVID-19 infected patients, a generalized procoagulable state similar to sepsis may exist rather than septic emboli [8]. Elevated concentration of inflammation and hypercoagulability markers such as C reactive protein and D dimers in patients with COVID-19 infection suggest an underlying hypercoagulable state. While none of these laboratory abnormalities are a contraindication to IV thrombolysis, previous studies conducted in non COVID-19 infected acute ischemic stroke patients demonstrated a higher rate of death or disability and post thrombolytic intracerebral hemorrhages in such patients [6]. Hepatic dysfunction manifesting as elevation in serum transaminases without coagulopathy or with coagulopathy (elevated prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), or reduced platelet count) can occur in patients with COVID-19 infection. Current guidelines specify certain eligibility thresholds based on elevated PT, INR, APTT, or reduced platelet counts although there is ambiguity regarding thresholds associated with greater risk or benefit with IV thrombolysis [7]. Additional tests for assessing coagulation profile such as thromboelastography and serum concentration of D dimers have been useful in sepsis and hepatic dysfunction and may be considered as needed. For patients with COVID-19 infection and other organ involvement, a detailed assessment of

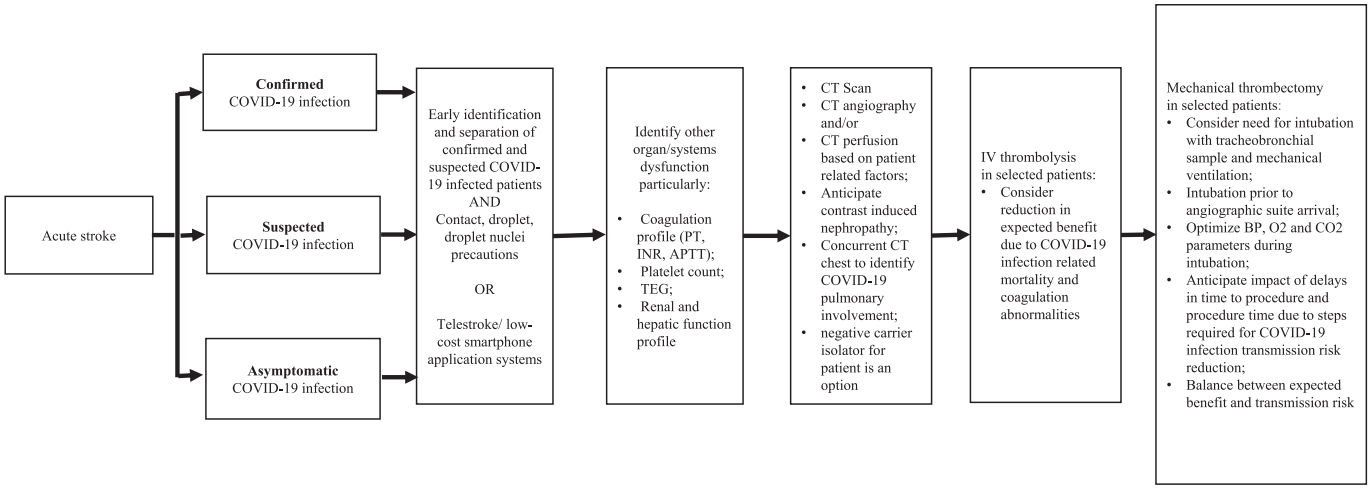

Fig. 1. Proposed workflow of hyper acute stroke care in era of COVID 19 pandemic. Adapted from [11] Abbreviations: PT: prothrombin time, INR: international normalized ratio, aPTT: activated partial thromboplastin time, TEG: thromboelastography, CT: computerized tomography, IV: intravenous, BP: blood pressure, O2: oxygen, CO2: carbon dioxide.

coagulation profile is preferable prior to decision regarding IV thrombolysis to determine risk benefit ratio.

Current guidelines recommend mechanical thrombectomy in acute ischemic stroke in patients ≥18 years who have a causative occlusion of the internal carotid artery or proximal middle cerebral artery and can be treated within 6 h of last known normal [7]. Mechanical thrombectomy is recommended in selected acute stroke patients within 6–24 h of last known normal but requires CT perfusion or magnetic resonance imaging to identify potentially salvageable tissue [7]. In addition to patient characteristics, the time interval between symptom onset and initiation of treatment and procedure time are important determinants of benefit of procedure. In the current era of COVID-19 pandemic there will be a new challenge in triage of these patients as suspected or known COVID-19 patients cannot be transferred rapidly to angiographic suites from emergency departments or from outside hospitals due to screening and exposure reduction requirements. Interfacility transfer may require special equipment and personnel which is likely to delay the procedure. Obtaining informed consents in light of "no visitor hospital policies" may require waiver of consent or remote electronic informed consent for such procedures. Due to expected challenges, IV thrombolysis in an isolation ward has been recommended preferentially in patients with acute myocardial infarction. In patients selected for mechanical thrombectomy, intubation, mechanical ventilation, and general anesthesia may be required in a relatively large proportion (if not all) of patients due to underlying COVID-19 related respiratory insufficiency and stroke related neurological deficits, and to reduce aerosol exposure and avoid unplanned intubation within angiographic unit. Tracheobroncholar sample may be acquired at time of intubation to confirm patient's diagnosis and infectious potential. Due to the additional precautions required in endotracheal intubation, open suctioning, and manual ventilation before intubation in COVID-19 infected patients, the intubation is best performed prior to arrival to the angiographic suite by an experienced team using appropriate protective gear and special equipment. Strict parameters for systolic blood pressure or mean arterial pressure and end tidal carbon dioxide need to be used to reduce the risk of death or disability in patients who require intubation and mechanical ventilation prior to mechanical thrombectomy in previous reports [9]. All health care professionals within the angiographic suite should wear surgical/medical masks, gloves, gown, and eye protection, such as a face shield or safety goggles at the minimum and a particulate filtering facepiece respirator if required. There may be limitations in interpersonal communication and technical comments imposed by personal protective equipment.

Mechanical thrombectomy procedures are performed in radiographic-fluoroscopic room, usually equipped with biplane floor-mounted and ceiling-mounted C-arm angiography system with two flat detectors mounted on a motorized rotating turntable. The patients are placed on a floor-mounted cantilevered carbon-fiber tabletop covered with special contoured foam mattress. The transmission of SARS-CoV-2 virus from contaminated environmental surfaces and noncritical equipment to health care workers and other patients is a serious concern because SARS-CoV-2 can survive in aerosol up to 3 h, on copper up to 4 h, on cardboard up to 24 h, on stainless steel metal and plastic surface up to 72 h [10]. Use of non-porous sterile coverings on all areas in procedure field is the currently acceptable procedure. A policy is required that identifies the principles of decontamination and disinfectants (different concentration and exposure time required for elimination of SARS-CoV-2 virus) for various categories of contaminated items (critical items from blood stream, semi-critical items from mucous membranes, and noncritical items from intact skin) and surfaces (high touch and low touch) when a patient with suspected or confirmed COVID-19 infection undergoes mechanical thrombectomy. A protocol for terminal clean must be developed if not already available to reduce and eliminate microbial contamination to avoid transfer of microorganisms to the next patient. Strategies to reduce anticipated longer procedure time due to new precautionary measures in acute ischemic patients undergoing mechanical thrombectomy need to be considered at institutional level. A negative-pressure rooms with anterooms for patients with airborne viral diseases is recommended with or without portable, industrial-grade high efficiency particulate air filter units. Although it is preferable to use negative pressure angiographic suites for mechanical thrombectomy, such angiographic suites do not exist in most institutions.

Comprehensive and designated stroke centers must anticipate new challenges because of mismatch between demand and resources. A deviation of resources towards service lines responsible for management of patients with COVID-19 infection may occur because of concurrent existence of other specialties in comprehensive and designated stroke centers. The high volume of elective neuroendovascular procedures incomprehensive stroke centers may require cancellation and deferral to preserve resources for acute stroke management. Transitional Care Units may be required to reduce the risk of transmission in post procedure period.

Prospective registries may help understand whether there are differences in stroke risk, manifestations, response to treatment strategies, and outcomes in patients with COVID-19 infection.

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