HHS Public Access

Author manuscript

Stroke. Author manuscript; available in PMC 2022 January 20.

Published in final edited form as:

Stroke. 2021 January ; 52(2): 729–734. doi:10.1161/STROKEAHA.120.033744.

Advances in Acute Stroke Treatment 2020

Joseph P Broderick, MD,

Departments of Neurology, University of Cincinnati Gairdner Neuroscience Institute, University of Cincinnati Academic Health Center, OH.

Michael D Hill, MD MSc FRCPC

Department of Clinical Neurosciences and Hotchkiss Brain Institute, University of Calgary and Foothills Medical Centre, Calgary, Alberta, CANADA

Subject terms

Ischemic stroke; intracerebral hemorrhage; cerebral venous sinus thrombosis; thrombolysis; endovascular thrombectomy; Covid19

Keywords

ischemic stroke; stroke management ischemia; intracerebral hemorrhage; thrombolysis; thrombectomy; Covid19

Introduction

In this past year, medicine has been dominated by the Covid19 pandemic. Acute stroke care and research has been affected both directly[1, 2] and indirectly. We present a summary and commentary on advances published and presented in 2020 ending with observations on Covid19 and stroke.

Endovascular thrombectomy (EVT) in Middle and Low-Income Countries

EVT has been shown to be a highly effective treatment in high-resource countries. The RESILIENT Trial performed at 12 public hospitals in Brazil demonstrated that EVT is also highly effective in a health care system with more constrained resources.[3] Infrastructure and support are needed for EVT in the developing world.

Acute Ischemic Stroke Thrombolysis and EVT

For a quarter century, thrombolysis has been a standard of care treatment for acute ischemic stroke. The withholding of intravenous alteplase seems anathema, but has now been challenged in patients with large artery occlusions arriving first at thrombectomy centres. The SKIP trial,[4] examined 204 Japanese patients with middle cerebral artery (MCA) or

Corresponding Author: Dr. Michael D Hill, Professor, Dept Clinical Neuroscience & Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary & Foothills Medical Centre, HBA 2939, Health Science Centre, 3330 Hospital Drive NW, Calgary, AB T2N4N1. CANADA, P: +1 403 210 7786, michael.hill@ucalgary.ca.

internal carotid artery (ICA) occlusions, half of whom were randomized to treatment with intravenous alteplase (0.6 mg/kg) prior to EVT and half to EVT alone. The trial did not meet its primary outcome of non-inferiority. The DIRECT-MT trial[5] enrolled 656 patients of whom half were randomized to intravenous alteplase (0.9 mg/kg) prior to EVT and half to EVT alone. The median time from randomization to groin puncture was 33.5 minutes. The trial met its non-inferiority margin (cOR 1.07, 0.81–1.40) with 36.4% in the EVT only group and 36.8% in the alteplase plus EVT group achieving mRS 0–2 at 90 days. Participants treated with EVT alone had lower percentages of successful reperfusion before thrombectomy (2.4% vs. 7.0%) and overall successful reperfusion (79.4% vs. 84.5%). Mortality at 90 days was 17.7% in the thrombectomy-alone group and 18.8% in the combination-therapy groups. In both trials, however, the non-inferiority margin was much larger than the minimal clinically important difference and so the trials were underpowered. Additional trials, MR-CLEAN-NoIV, SWIFT-DIRECT, and DIRECT-SAFE are ongoing.

A quarter of patients with ICA or M1-MCA occlusions in the INTERRSeCT study had thrombus migration into a distal segment resulting in poorer outcomes compared to complete recanalization or no change in recanalization. Registry data from California identified the challenge of distal embolization occurring in a quarter of patients resulting in distal emboli that were not possible to address with EVT.[6] Both studies confirm data from the MR-CLEAN registry.[7] Similarly, data from the ESCAPE trial showed early recanalization rates of only 6% in the EVT arm at a median of 50 minutes after the start of IV alteplase infusion. In the control arm, recanalization was observed, on CTA completed a median of ~4.5h after the start of intravenous alteplase infusion, in 37% of patients.[8] The EXTEND-IA-TNK part 2 study compared two doses of tenecteplase, 0.25 vs. 0.4 mg/kg, among patients with large vessel occlusion, eligible for EVT.[9] The primary outcome was early recanalization (not reperfusion) defined at the first angiographic run of the EVT procedure. There was no difference in outcome between the two doses but the study confirmed prior results from EXTEND-IA TNK part 1,[10] of an early recanalization rate of 20% at an average of 46.5 minutes from treatment with tenecteplase to imaging. Finally, a pooled individual patient meta-analysis of trials examining patients with stroke-with-unknown-onset, who were selected by MR imaging (either DWI-FLAIR mismatch or MR perfusion imaging, showed that intravenous alteplase treatment was superior to placebo when assessed at 90 days.[11]

Together these data provide empiric evidence and quantitative understanding of the in vivo mechanisms of intravenous thrombolysis, further demonstrating that patient selection is increasingly based on imaging and not time, and that thrombolytic agents require time to work. In a majority of patients with large vessel occlusion, thrombolysis alone will be unsuccessful during the critical time window when reperfusion will effectively salvage the ischemic tissue. In addition, thrombolysis can, in a minority of patients with large vessel occlusions, make the situation worse due to thrombus migration. Very rapid EVT possibly obviates any additional benefit of combined intravenous thrombolysis and EVT, but it remains unknown if an incremental benefit of combined therapy may emerge due to thrombolytic action on distal emboli, on incomplete reperfusion, on the microcirculation, or in situations where EVT proves to be unsuccessful. In contrast, a 20% target vessel recanalization rate within 45 minutes after thrombolysis is clinically meaningful, particularly

in the drip and ship paradigm. Treatment with tenecteplase at 0.25 mg/kg (the dose seems settled now[9, 12–14]) is not ready for widespread usage at present but more evidence will accrue from ongoing trials (TASTE, TEMPO-2, NORTEST-2, ACT, TWIST) over the next two years. The issue of withholding thrombolysis, is much less relevant when patients arrive at hospitals which do not perform EVT and so far the data do not justify withholding thrombolysis generally. At the end of 2020 it remains clear that the goal of acute ischemic stroke treatment is reperfusion as quickly as possible, whether that is achieved by going directly to EVT in selected patients or with combined thrombolysis and EVT in most patients.

EVT in Minor Ischemic Stroke, Basilar Artery Occlusion and Parenteral Antiplatelet Agents

Two cohort studies and a meta-analysis examining whether patients with mild symptoms (typically NIHSS 0–5) and a proximal large vessel occlusion should be treated with EVT reported similar outcomes between patients treated medically and those treated with EVT.[15–17] Randomized trials are underway to assess this question but it will always be more challenging to show a treatment effect on clinical outcomes when symptoms are mild given the ceiling effects on outcome scores. Selection of the specific populations of patients with LVO and only minor symptoms who will benefit from EVT remains an important research goal.

Large registries suggest the EVT is superior to medical therapy for basilar artery occlusion,[18] but this has not yet been shown in trials. The open-label BEST trial randomized patients with basilar artery occlusion to EVT and best medical management versus best medical management alone. The trial was terminated early after 131 patients because of poor recruitment and high frequency of cross-over. In the intention-to-treat analysis, there was no evidence of a difference in the proportion of participants with mRS 0–3 at 90 days according to treatment (28 [42%] of 66 patients in the intervention group vs 21 [32%] of 65 in the control group; adjusted odds ratio [OR] 1·74, 95% CI 0·81–3·74).[19] Further data from the BASICS trial have also reported a neutral outcome, with a trend toward better outcomes in the EVT group for those with higher NIHSS (Schonewille W. Personal communication and presented at ESOC-WSC 2020). Discrepancy in outcomes between cohort studies and randomized trials suggest both that selection bias exists in the cohort studies and that we have yet to identify the target subgroup of basilar artery occlusion patients who stand to benefit from EVT.

Intravenous or intra-arterial tirofiban as an adjunct prior to or as rescue treatment during EVT treatment has received ongoing attention, particularly in Asia but no data from larger randomized trials are available yet.[20, 21] Mechanistically, the benefits of parenteral antiplatelet agents may follow the same paradigm as that seen in acute coronary syndromes and be of most utility in large vessel occlusion stroke due to intracranial atherosclerotic disease.

Cytoprotection and Adjuvant Therapies for Ischemic Stroke Reperfusion

The evolution of treatments for ischemic stroke due to LVO has resulted in a true human ischemia-reperfusion model, the same model in which pre-clinical demonstration of cytoprotection (or neuroprotection) has been proven for multiple compounds. The ESCAPE-NA1 trial assessed the peptide, nerinetide (previously called NA-1, TatNR2b9c), among 1105 patients with anterior circulation LVO undergoing EVT.[22] The trial stratified randomization by alteplase treatment but was neutral overall. However, there was an alteplase-by-nerinetide treatment interaction, such that patients in the alteplase stratum showed no benefit, but patients in the no-alteplase stratum showed a 9.5% absolute risk benefit (RR = 1·19, CI_{95} 1·01 to 1·41). This was a post-hoc test of interaction but was biologically supported by pharmacokinetic studies which suggest that there was an indirect effect of alteplase on cleavage of nerinetide in vivo. If the results can be confirmed in the ESCAPE-NEXT trial, this will give hope to other compounds that are being developed using the same paradigm. These include the modified activated protein C molecule, 3K3A-APC, which has already undergone assessment in the phase 2 Rhapsody study.[23] Simple molecules such as high-dose uric acid[24, 25] may be assessed in future trials.

Intracerebral Hemorrhage (ICH)

ICH remains the most challenging stroke type. STOP-AUST randomized 100 patients with acute ICH <70 cc, a spot sign on CT angiography to receive intravenous tranexamic acid 1 g over 10 min followed by 1 g over 8 h or matching placebo, started within 4·5 h of symptom onset and within 1 hour of the qualifying CT scan.[26] There was no observed difference in the primary surrogate outcome of hemorrhage growth [OR = 0·72, CI_{95} 0·32–1·59]. A post-hoc analysis of the ATACH-2 study reported that dropping the blood pressure by very large absolute amounts (>220 mmHg systolic down to <140mmHg systolic) may result in both poorer neurological outcomes and a greater chance of acute renal failure.[27] However, a subgroup of patients (about 1/3rd of the trial population), treated within 2 hours of onset showed reduced hematoma growth and better outcomes with intensive blood pressure lowering comparing to control.[28] New studies are planned for ICH that will focus on the ultra-early treatment window, including a return to the assessment of recombinant factor VIIa within two hours of onset.[1]

Cortical Venous Sinus Thrombosis (CVST)

CVST is the least common form of stroke and randomized data on CVST management, both acute and chronic, are sparse. The TOACT study (n=67), assessing endovascular treatment (mechanical with or without local thrombolytic drug infusion) vs. best medical care was conducted in Europe and China.[29] There was no difference in outcomes at 1 year with two-thirds of the population in both groups achieving mRS 0–1 (relative risk ratio, 0.99; CI_{95}, 0.71–1.38). Given its low prevalence relative to other stroke types, continued global collaboration on CVST trials is needed.

Covid19

While some initial case reports suggested that a pro-thrombotic state occurs in some patients with Covid19 that may manifest as large vessel occlusion, population-based data have yet to report an increased incidence of ischemic stroke.[30, 31] In fact, stroke admissions may have fallen overall.[32, 33] Finally, we recommend several publications that have addressed acute stroke care process to maximize safety for patients and health care personnel.[34–37]

Acknowledgement

The authors would like to acknowledge input from many members of the stroke community who sent suggestions and comments by email.

Disclosures

Dr Broderick reports funding from the National Institutes of Health (NINDS and NHLBI) and other support from Genentech during the conduct of the study; other support from Ono Pharmaceuticals and other support from Novo Nordisk outside the submitted work.

Dr Hill reports grants from NoNo Inc, grants from CIHR, grants from Medtronic LLC, and grants from Boehringer Ingelheim Canada Ltd outside the submitted work; in addition, Dr Hill has a patent to US Patent office Number: 62/086,077 issued and licensed; and Director at Circle NVI; Director at the Canadian Stroke Consortium; Director and the Canadian Neuroscience Federation.

Funding

There were no funding sources for this manuscript

Abbreviations and Acronyms

LVO	large vessel occlusion
EVT	endovascular thrombectomy/treatment
ICH	intracerebral hemorrhage
CVST	cerebral venous sinus thrombosis
CT	computed tomography
MR	magnetic resonance
DWI	diffusion weighted imaging
FLAIR	fluid attenuated inversion recovery
CTA	CT angiography
NIHSS	National Institutes of Health Stroke Scale
RESILIENT	Randomization of Endovascular Treatment With Stent-retriever and/or Thromboaspiration vs. Best Medical Therapy in Acute Ischemic Stroke Due to Large VEssel OcclusioN Trial

SKIP	Randomised study of endovascular therapy with vs without intravenous tissue plasminogen activator in acute stroke with ICA and M1 occlusion
DIRECT-MT	Direct Intra-arterial Thrombectomy in Order to Revascularize AIS Patients With Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: a Multicentre Clinical Trial
MR-CLEAN NoIV	Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands No IV thrombolysis study
SWIFT-DIRECT	Solitaire™ With the Intention For Thrombectomy Plus Intravenous t-PA vs DIRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke
DIRECT-SAFE	Randomized Controlled Trial of DIRECT Endovascular Clot Retrieval vs Standard Bridging Thrombolysis With Endovascular Clot Retrieval Within 4.5 Hours of Stroke Onset
INTERRSeCT	Identifying New Approaches to Optimize Thrombus Characterization for Predicting Early Recanalization and Reperfusion With IV Alteplase and Other Treatments Using Serial CT Angiography study
BEST	Acute Basilar Artery Occlusion: Endovascular Interventions vs Standard Medical Treatment
BASICS	Basilar Artery International Cooperation Study
ESCAPE	Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times study
ESCAPE-NA1	Extension of Stroke Care by Added neuroProtection to Endovascular treatment
ESCAPE-NEXT	Efficacy and Safety of Nerinetide in Participants With Acute Ischemic Stroke Undergoing Endovascular Thrombectomy Excluding Thrombolysis
EXTEND-IA TNK	Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial Using Intravenous Tenecteplase study
TASTE	Tenecteplase Versus Alteplase for Stroke Thrombolysis Evaluation Trial

TEMPO-2	Multicentre, Prospective Randomized Open Label, Blinded-endpoint (PROBE) Controlled Trial of Thrombolysis With Low Dose Tenecteplase (TNK-tPA) Versus Standard of Care in Minor Ischemic Stroke With Proven Acute Symptomatic Occlusion
NORTEST-2	Norwegian Tenecteplase Stroke Trial 2: A Randomised Trial of Tenecteplase vs. Alteplase in Acute Ischemic Stroke
ACT	Alteplase Compared to Tenecteplase in Patients With Acute Ischemic Stroke: QuICR & OPTIMISE Registry Based Pragmatic Randomized Controlled Trial
TWIST	Tenecteplase in Wake-up Ischaemic Stroke Trial (TWIST). A Randomised-controlled Trial of Thrombolytic Treatment With Tenecteplase for Acute Ischaemic Stroke Upon Awakening
TOACT	Thrombolysis or Anticoagulation for Cerebral Venous Thrombosis study
STOP-AUST	Spot Sign and Tranexamic Acid On Preventing ICH Growth - AUStralasia Trial
ATACH-2	Antihypertensive Treatment of Acute Cerebral Hemorrhage 2 study

References

1. Broderick JP, Elm JJ, Janis LS, Zhao W, Moy CS, Dillon CR, Chimowitz MI, Sacco RL, Cramer SC, Wolf SL, et al. National Institutes of Health StrokeNet During the Time of COVID-19 and Beyond. Stroke. 2020;51:2580–2586. [PubMed: 32716819]
2. Lyden PD. Stroke, Research and Science in the Time of COVID. Stroke. 2020;51:2613–2614. [PubMed: 32755344]
3. Martins SO, Mont'Alverne F, Rebello LC, Abud DG, Silva GS, Lima FO, Parente BSM, Nakiri GS, Faria MB, Frudit ME, et al. Thrombectomy for Stroke in the Public Health Care System of Brazil. N Engl J Med. 2020;382:2316–2326. [PubMed: 32521133]
4. Suzuki K, Kimura K, Takeuchi M, Morimoto M, Kanazawa R, Kamiya Y, Shigeta K, Ishii N, Takayama Y, Koguchi Y, et al. The randomized study of endovascular therapy with versus without intravenous tissue plasminogen activator in acute stroke with ICA and M1 occlusion (SKIP study). Int J Stroke. 2019;14:752–755. [PubMed: 30924762]
5. Yang P, Zhang Y, Zhang L, Treurniet KM, Chen W, Peng Y, Han H, Wang J, Wang S, Yin C, et al. Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke. N Engl J Med. 2020.
6. Flint AC, Avins AL, Eaton A, Uong S, Cullen SP, Hsu DP, Edwards NJ, Reddy PA, Klingman JG, Rao VA, et al. Risk of Distal Embolization From tPA (Tissue-Type Plasminogen Activator) Administration Prior to Endovascular Stroke Treatment. Stroke. 2020;51:2697–2704. [PubMed: 32757749]
7. Alves HC, Treurniet KM, Jansen IGH, Yoo AJ, Dutra BG, Zhang G, Yo L, van Es ACGM, Emmer BJ, van den Berg R, et al. Thrombus Migration Paradox in Patients With Acute Ischemic Stroke. Stroke. 2019;50:3156–3163. [PubMed: 31597552]

8. Ospel JM, Singh N, Almekhlafi MA, Menon BK, Butt A, Poppe AY, Jadhav A, Silver FL, Shah R, Dowlatshahi D, et al. Early Recanalization With Alteplase in Stroke Because of Large Vessel Occlusion in the ESCAPE Trial. Stroke. 2020:STROKEAHA120031591.

9. Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, Yan B, Bush SJ, Thijs V, Scroop R, et al. Effect of Intravenous Tenecteplase Dose on Cerebral Reperfusion Before Thrombectomy in Patients With Large Vessel Occlusion Ischemic Stroke: The EXTEND-IA TNK Part 2 Randomized Clinical Trial. JAMA. 2020;323:1257–1265. [PubMed: 32078683]

10. Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, Yan B, Bush SJ, Dewey HM, Thijs V, et al. Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke. N Engl J Med. 2018;378:1573–1582. [PubMed: 29694815]

11. Thomalla G, Boutitie F, Ma H, Koga M, Ringleb P, Schwamm LH, Wu O, Bendszus M, Bladin CF, Campbell BCV, et al. Intravenous alteplase for stroke with unknown time of onset guided by advanced imaging: systematic review and meta-analysis of individual patient data. Lancet. 2020;396:1574–1584. [PubMed: 33176180]

12. Coutts SB, Dubuc V, Mandzia J, Kenney C, Demchuk AM, Smith EE, Subramaniam S, Goyal M, Patil S, Menon BK, et al. Tenecteplase-tissue-type plasminogen activator evaluation for minor ischemic stroke with proven occlusion. Stroke. 2015;46:769–74. [PubMed: 25677596]

13. Parsons M, Spratt N, Bivard A, Campbell B, Chung K, Miteff F, O'Brien B, Bladin C, McElduff P, Allen C, et al. A randomized trial of tenecteplase versus alteplase for acute ischemic stroke. N Engl J Med. 2012;366:1099–107. [PubMed: 22435369]

14. Huang X, Cheripelli BK, Lloyd SM, Kalladka D, Moreton FC, Siddiqui A, Ford I and Muir KW. Alteplase versus tenecteplase for thrombolysis after ischaemic stroke (ATTEST): a phase 2, randomised, open-label, blinded endpoint study. Lancet Neurol. 2015;14:368–76. [PubMed: 25726502]

15. Volny O, Zerna C, Tomek A, Bar M, Rocek M, Padr R, Cihlar F, Nevsimalova M, Jurak L, Havlicek R, et al. Thrombectomy vs medical management in low NIHSS acute anterior circulation stroke. Neurology. 2020.

16. Seners P, Perrin C, Lapergue B, Henon H, Debiais S, Sablot D, Girard Buttaz I, Tamazyan R, Preterre C, Laksiri N, et al. Bridging Therapy or IV Thrombolysis in Minor Stroke with Large Vessel Occlusion. Ann Neurol. 2020;88:160–169. [PubMed: 32350929]

17. Zhao Y, Song Y, Guo Y, Li Y, Zhang Y, Ma P, Li G and Li F. Endovascular Thrombectomy VS. Medical Treatment for Mild Stroke Patients: A Systematic Review and Meta-Analysis. J Stroke Cerebrovasc Dis. 2020;29:105258. [PubMed: 32992178]

18. Zi W, Qiu Z, Wu D, Li F, Liu H, Liu W, Huang W, Shi Z, Bai Y, Liu Z, et al. Assessment of Endovascular Treatment for Acute Basilar Artery Occlusion via a Nationwide Prospective Registry. JAMA Neurol. 2020;77:561–573. [PubMed: 32080711]

19. Liu X, Dai Q, Ye R, Zi W, Liu Y, Wang H, Zhu W, Ma M, Yin Q, Li M, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. Lancet Neurol. 2020;19:115–122. [PubMed: 31831388]

20. Yang J, Wu Y, Gao X, Bivard A, Levi CR, Parsons MW, Lin L and Group† IS. Intraarterial Versus Intravenous Tirofiban as an Adjunct to Endovascular Thrombectomy for Acute Ischemic Stroke. Stroke. 2020;51:2925–2933. [PubMed: 32933416]

21. Fu Z, Xu C, Liu X, Wang Z and Gao L. Safety and Efficacy of Tirofiban in Acute Ischemic Stroke Patients Receiving Endovascular Treatment: A Meta-Analysis. Cerebrovasc Dis. 2020;49:442–450. [PubMed: 32731250]

22. Hill MD, Goyal M, Menon BK, Nogueira RG, McTaggart RA, Demchuk AM, Poppe AY, Buck BH, Field TS, Dowlatshahi D, et al. Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1): a multicentre, double-blind, randomised controlled trial. Lancet. 2020;395:878–887. [PubMed: 32087818]

23. Lyden P, Pryor KE, Coffey CS, Cudkowicz M, Conwit R, Jadhav A, Sawyer RN, Claassen J, Adeoye O, Song S, et al. Final Results of the RHAPSODY Trial: A Multi-Center, Phase 2 Trial Using a Continual Reassessment Method to Determine the Safety and Tolerability of 3K3A-APC, A Recombinant Variant of Human Activated Protein C, in Combination with Tissue Plasminogen Activator, Mechanical Thrombectomy or both in Moderate to Severe Acute Ischemic Stroke. Ann Neurol. 2019;85:125–136. [PubMed: 30450637]

24. Chamorro A, Amaro S, Castellanos M, Segura T, Arenillas J, Martí-Fábregas J, Gállego J, Krupinski J, Gomis M, Cánovas D, et al. Safety and efficacy of uric acid in patients with acute stroke (URICO-ICTUS): a randomised, double-blind phase 2b/3 trial. Lancet Neurol. 2014;13:453–60. [PubMed: 24703208]
25. Chamorro Á, Amaro S, Castellanos M, Gomis M, Urra X, Blasco J, Arenillas JF, Román LS, Muñoz R, Macho J, et al. Uric acid therapy improves the outcomes of stroke patients treated with intravenous tissue plasminogen activator and mechanical thrombectomy. Int J Stroke. 2017;12:377–382. [PubMed: 28345429]
26. Meretoja A, Yassi N, Wu TY, Churilov L, Sibolt G, Jeng JS, Kleinig T, Spratt NJ, Thijs V, Wijeratne T, et al. Tranexamic acid in patients with intracerebral haemorrhage (STOP-AUST): a multicentre, randomised, placebo-controlled, phase 2 trial. Lancet Neurol. 2020;19:980–987. [PubMed: 33128912]
27. Qureshi AI, Huang W, Lobanova I, Barsan WG, Hanley DF, Hsu CY, Lin CL, Silbergleit R, Steiner T, Suarez JI, et al. Outcomes of Intensive Systolic Blood Pressure Reduction in Patients With Intracerebral Hemorrhage and Excessively High Initial Systolic Blood Pressure: Post Hoc Analysis of a Randomized Clinical Trial. JAMA Neurol. 2020.
28. Li Q, Warren AD, Qureshi AI, Morotti A, Falcone GJ, Sheth KN, Shoamanesh A, Dowlatshahi D, Viswanathan A and Goldstein JN. Ultra-Early Blood Pressure Reduction Attenuates Hematoma Growth and Improves Outcome in Intracerebral Hemorrhage. Ann Neurol. 2020;88:388–395. [PubMed: 32453453]
29. Coutinho JM, Zuurbier SM, Bousser MG, Ji X, Canhão P, Roos YB, Crassard I, Nunes AP, Uyttenboogaart M, Chen J, et al. Effect of Endovascular Treatment With Medical Management vs Standard Care on Severe Cerebral Venous Thrombosis: The TO-ACT Randomized Clinical Trial. JAMA Neurol. 2020;77:966–973. [PubMed: 32421159]
30. 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. [PubMed: 32343504]
31. Nannoni S, de Groot R, Bell S and Markus HS. Stroke in COVID-19: A systematic review and meta-analysis. Int J Stroke. 2020:1747493020972922. [PubMed: 33103610]
32. Sacco S, Ricci S, Ornello R, Eusebi P, Petraglia L, Toni D and Organization IS. Reduced Admissions for Cerebrovascular Events During COVID-19 Outbreak in Italy. Stroke. 2020;51:3746–3750. [PubMed: 33059543]
33. Kansagra AP, Goyal MS, Hamilton S and Albers GW. Collateral Effect of Covid-19 on Stroke Evaluation in the United States. N Engl J Med. 2020;383:400–401. [PubMed: 32383831]
34. Nguyen TN, Abdalkader M, Jovin TG, Nogueira RG, Jadhav AP, Haussen DC, Hassan AE, Novakovic R, Sheth SA, Ortega-Gutierrez S, et al. Mechanical Thrombectomy in the Era of the COVID-19 Pandemic: Emergency Preparedness for Neuroscience Teams: A Guidance Statement From the Society of Vascular and Interventional Neurology. Stroke. 2020;51:1896–1901. [PubMed: 32347790]
35. 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. [PubMed: 32352910]
36. Wira CR, Goyal M, Southerland AM, Sheth KN, McNair ND, Khosravani H, Leonard A, Panagos P, AHA/ASA Stroke Council Science Subcommittees: Emergency Neurovascular Care (ENCC) TlatNIC and Council aobotSNSSotAACaSN. Pandemic Guidance for Stroke Centers Aiding COVID-19 Treatment Teams. Stroke. 2020;51:2587–2592. [PubMed: 32716826]
37. Khosravani H, Rajendram P, Notario L, Chapman MG and Menon BK. Protected Code Stroke: Hyperacute Stroke Management During the Coronavirus Disease 2019 (COVID-19) Pandemic. Stroke. 2020;51:1891–1895. [PubMed: 32233980]