Telemedicine in Prehospital Acute Stroke Care: An Expanding Infrastructure for Treatment and Research

Paul J. Derry, PhD; Pitchaiah Mandava, MD, PhD, MSEE; Thomas A. Kent, MD

After years of disappointments, including the failure of several neuroprotectants and the first generation of endovascular therapies to improve outcomes, we are in a period of rapid evolution in the treatment of acute ischemic stroke. Evidence for benefit of the latest generation of endovascular stent-retriever devices[1] has reenergized the stroke community, suggesting that their efforts to enhance systems of care, not only within the treatment facility itself, but also community wide, might be realizing their potential. Although it is generally thought that the sooner clot-directed therapy is initiated, the better,[2] there appears to be a subgroup of patients in whom endovascular intervention offers some outcome advantage, even at longer time windows.[3–5] Although much work has gone into identifying factors that may influence the time window in groups of patients, with the presence of collateral flow[6] and acute hyperglycemia[7,8] among factors that consistently appear to influence outcome, we still do not have a way to assess how much time is left in a specific individual to derive maximal benefit, so it seems reasonable that unnecessary delays be minimized.

The push for faster initiation of stroke therapy has moved its way to the ambulance by way of mobile stroke units (MSUs),[9] and onto the cellular broadband network, as nicely described and tested by Geisler et al in this issue of the *Journal of the American Heart Association* (*JAHA*).[10] The possibility of a remote connection to a stroke expert rather than one physically present in the MSU could have the advantage of broader availability of expertise to the MSU.[11] Although the ultimate value of MSUs is still being investigated, this study adds to evidence[11] of their feasibility and suggests that the practice could be more widely implemented and tested. In this study, there was good diagnostic agreement between a stroke expert physically present in the MSU and an expert connected by the cellular broadband remotely, mostly at a single hospital site. Most of the time, the MSU was able to find a place for successful transmission, although poor cellular connection was among the factors that caused a remote failure rate of ≈10%. More important, the treatment decision to administer recombinant tPA (tissue-type plasminogen activator) seemed to be in good agreement, with only 2 disagreements about whether to administer tPA of 90 total treatment decisions made; neither disagreement was because of an issue with the remote connection. Not unexpectedly, there was disagreement among the experts in one case as to whether tPA was contraindicated (herein, because of an international normalized ratio of 1.6). In the other case, the tPA time window elapsed for the remote neurologist but not for the one physically present in the MSU. Of some concern in terms of generalization is the low mean National Institutes of Health Stroke Scale stroke severity reported in this population, a mean between 2 and 3, depending on which neurologist did the examination (the National Institutes of Health Stroke Scale is a scale from 0 [no deficit] to 42). Whether the same interrater agreement will occur in a more severely affected patient using this group's MSU is not known. Given the current push for rapid initiation of endovascular therapy for emergent large-vessel occlusion, this study does not provide the information needed to know whether cellular broadband will support an accurate assessment in such patients, who typically have higher initial National Institutes of Health Stroke Scale scores. However, the overall MSU literature is expanding and can likely address this question. Moreover, it seems probable, in our opinion, that more severe deficits will be more readily detected remotely, although this still needs to be tested.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston, TX (P.J.D., T.A.K.); Analytical Software and Engineering Research Laboratory, Department of Neurology, Baylor College of Medicine, Michael E. DeBakey VA Medical Center, Houston, TX (P.M.); and Department of Neurology and Institute of Academic Medicine, Houston Methodist Hospital, Houston, TX (T.A.K.).

Correspondence to: Thomas A. Kent, MD, Texas A&M Health Science Center–Houston Campus, 2121 W Holcombe Blvd, Ste 1004, Houston, TX 77030. E-mail: tkent@tamhsc.edu

J Am Heart Assoc. 2019;8:e012259. DOI: 10.1161/JAHA.119.012259.

It is particularly interesting to us, who have lived through the time lags in applying new practices, that the MSU has been introduced as widely as it has so quickly. Although it took more than a decade to incorporate thrombolysis into routine stroke care, more recent therapies provide a contrast in the speed of implementation before conclusive evidence of their benefit, including the growing presence of MSUs. Indeed, as our group suggested as long ago as 2007,[12] the first generation of endovascular interventions for emergent large-vessel occlusion was incorporated into practice too quickly, using techniques that had not been shown to actually improve outcomes. After a slew of negative results,[13] its use declined rapidly, but then rapidly reemerged with the new generation of endovascular devices as one clinical trial after another showed their advantage over usual practice.

What changed between these 2 eras? In our view, the primary reason for the change in the pace of incorporation is the efforts of the broad stroke community, spanning hospital administration, stroke clinicians, the Emergency Medical System, and community educators, to successfully demonstrate that it is possible to reduce delays and maybe even improve outcomes. What these systems of care now provide is the infrastructure in which modifications of care practices can be tested, at least in the more highly developed urban centers. Will every new approach and therapy prove beneficial? Probably no, particularly as interventions are expanded to those patients who do not qualify for currently available therapies and, therefore, likely have complicating factors. Will every effort to enhance the speed in which treatment is provided improve outcomes? Again, probably no. Rapid diagnosis exposes the limits of our diagnostic ability; hence, the percentage of patients with stroke mimics and spontaneous resolution (ie, transient ischemic attacks) increases if the focus is solely on speed. Although some contend the risk of harm for treating a stroke mimic or a transient ischemic attack can be favorably weighed against the overall benefit,[14] these are issues that require continued attention. But the presence of this infrastructure is a huge change that hopefully will facilitate testing these and other important real-world questions.

What about the future of the cellular technology? Beginning as a noisy analog voice communications mode, wireless telephony has become completely digital and is able to serve not only voice but data as well using 3G and 4G technologies. The incorporation of data into cellular communications has created the infrastructure needed to transmit and receive real-time video. The data reported herein, from the TeDir (TeleDiagnostics in prehospital emergency medicine) trial by Geisler et al,[10] represent a logical extension to the capabilities of cellular telephony networks by enabling consulting physicians to work side by side with remote paramedics without the necessity for a separate communications network, thereby lowering the total cost of implementing telestroke care and potentially enabling more municipalities to roll out such systems in their own fire and ambulance services.

In the 5 years since the TeDir trial concluded, much has been made about the advent of 5G wireless services, which promise higher speeds to enable better video streaming and allow for more connected devices than on existing 4G networks. In addition, the availability of the more efficient H.265 video codec may enable higher-quality video (thus improving quality scores) while using the same amount of bandwidth necessary for a similar stream of H.264-encoded video that the authors report.[15] The authors discuss some of the limitations of the Deutsche Telekom network as points that could use improvement. For instance, some video sessions were repeatedly dropped because of poor-quality connections. With the rollout of 5G, these problems may become less severe, especially in metropolitan areas. However, some dead areas may remain, especially inside buildings, because of the limited propagation distance of millimeter wave radio frequency signals.[16] A rapid "failover," or switching to an audio-only channel, might be able to mitigate the problems caused by interruptions in video, but how applicable that would be to the MSU is not clear.

Even with the roll out of 5G, rural communities may continue to encounter problems with telestroke over cellular because wireless communication services to rural communities largely rely on low-band (longer-wavelength) cellular radio frequencies that can cover wider areas from a single point but do not necessarily provide the same speeds that higher-frequency signaling can achieve, making telestroke over cellular a more difficult endeavor. In 2018, the Federal Communications Commission found that ≈15 million Americans were outside of service areas that offered 10-megabit per second download speeds.[17] It will likely not be economically viable to provide the same level of cellular service per square as urban areas simply because of a lack of density. MSU routing algorithms that focus on providing a certain level of video service by navigating to faster cellular service on the way to the hospital might be able to mitigate some of those difficulties. And rapid failover to lower bandwidth communication methods while en route to the hospital may ultimately still be necessary. Reliability of the network is likely to be a constant concern as the MSU and networks are expanded.

In addition to the change in the technology to 5G, there is an evolution in the thinking of the role of tPA itself in stroke management in this era of endovascular therapy and, therefore, the advantage of more rapid initiation of treatment in an MSU. A series of reanalyses of existing data sets from trials or case series on the benefit of treatment with tPA before initiation of endovascular therapy appear to be equivocal as to the benefit of prior therapy with tPA[18,19] and, therefore, in our opinion, should continue to be investigated. Our own preliminary analysis of published stent-retriever endovascular trials found that there were better outcomes overall in those trials with a higher incidence of administration of tPA before endovascular therapy.[20] This analysis was complicated by faster treatment in patients who received tPA, and the results, therefore, are not conclusive. Also, this group of patients eligible for endovascular intervention was not highly represented in the current study,[10] given their low stroke severity. So, although the conclusions of this study may be limited to a relatively narrow question about the feasibility of remote assessment in an MSU of mostly mildly affected patients with stroke, the existence of this cellular MSU infrastructure itself will lend itself to the potential for testing these important ongoing questions. We can conclude that, although additional outcomes and cost-effectiveness research is certainly needed, telestroke over cellular represents an exciting application of wireless communications and its roll out may ultimately prove to be useful in improving stroke outcomes across the globe.

Sources of Funding

Kent is supported, in part, by National Institutes of Health R01NS094535, The State of Texas Lone Star Stroke Consortium, and Welch Foundation Grant BE-0048.

Disclosures

T.A.K. and P.M. own the copyright to predicts analytical software without any commercial interest.

References

1. Gill R, Schneck MJ. The use of stent retrievers in acute ischemic stroke. *Expert Rev Neurother*. 2016;16:969–981.
2. Marler JR, Tilley BC, Lu M, Brott TG, Lyden PC, Grotta JC, Broderick JP, Levine SR, Frankel MP, Horowitz SH, Haley EC Jr, Lewandowski CA, Kwiatowski TP. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. *Neurology*. 2000;55:1649–1655.
3. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, Davalos A, Majoie CB, van der Lugt A, de Miguel MA, Donnan GA, Roos YB, Bonafe A, Jahan R, Diener HC, van den Berg LA, Levy EI, Berkhamer OA, Pereira VM, Rempel J, Millan M, Davis SM, Roy D, Thornton J, Roman LS, Ribo M, Beumer D, Stouch B, Brown S, Campbell BC, van Oostenbrugge RJ, Saver JL, Hill MD, Jovin TG; 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.
4. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA, Hassan AE, Millan M, Levy EI, Mitchell P, Chen M, English JD, Shah QA, Silver FL, Pereira VM, Mehta BP, Baxter BW, Abraham MG, Cardona P, Veznedaroglu E, Hellinger FR, Feng L, Kirmani JF, Lopes DK, Jankowitz BT, Frankel MR, Costalat V, Vora NA, Yoo AJ, Malik AM, Furlan AJ, Rubiera M, Aghaebrahim A, Olivot JM, Tekle WG, Shields R, Graves T, Lewis RJ, Smith WS, Liebeskind DS, Saver JL, Jovin TG; DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378:11–21.
5. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, Sarraj A, Kasner SE, Ansari SA, Yeatts SD, Hamilton S, Mlynash M, Heit JJ, Zaharchuk G, Kim S, Carrozzella J, Palesch YY, Demchuk AM, Bammer R, Lavori PW, Broderick JP, Lansberg MG; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378:708–718.
6. Sheth SA, Sanossian N, Hao Q, Starkman S, Ali LK, Kim D, Gonzalez NR, Tateshima S, Jahan R, Duckwiler GR, Saver JL, Vinuela F, Liebeskind DS; UCLA Collateral Investigators. Collateral flow as causative of good outcomes in endovascular stroke therapy. *J Neurointerv Surg*. 2016;8:2–7.
7. Mandava P, Martini SR, Munoz M, Dalmeida WV, Sarma AK, Anderson JA. Hyperglycemia worsens outcome after rt-PA primarily in the large-vessel occlusive stroke subtype. *Transl Stroke Res*. 2014;5:519–525.
8. Osei E, den Hertog HM, Berkhemer OA, Fransen PSS, Roos Y, Beumer D, van Oostenbrugge RJ, Schonewild WJ, Boiten J, Zandbergen AAM, Koudstaal PJ, Dippel DWJ; MR CLEAN Investigators. Admission glucose and effect of intra-arterial treatment in patients with acute ischemic stroke. *Stroke*. 2017;48:1299–1305.
9. Fassbender K, Grotta JC, Walter S, Grunwald IQ, Ragoschke-Schumm A, Saver JL. Mobile stroke units for prehospital thrombolysis, triage, and beyond: benefits and challenges. *Lancet Neurol*. 2017;16:227–237.
10. Geisler F, Kunz A, Winter B, Rozanski M, Waldschmidt C, Weber JE, Wendt M, Zieschang K, Ebinger M, Audebert HJ; Stroke Emergency Mobile (STEMO) Consortium. Telemedicine in prehospital acute stroke care. *J Am Heart Assoc*. 2019;8:e011729. DOI: 10.1161/JAHA.118.011729.
11. Wu TC, Parker SA, Jagolino A, Yamal JM, Bowry R, Thomas A, Yu A, Grotta JC. Telemedicine can replace the neurologist on a mobile stroke unit. *Stroke*. 2017;48:493–496.
12. Mandava P, Kent TA. Intra-arterial therapies for acute ischemic stroke. *Neurology*. 2007;68:2132–2139.
13. Pierot L, Gralla J, Cognard C, White P. Mechanical thrombectomy after IMS III, synthesis, and MR-RESCUE. *AJNR Am J Neuroradiol*. 2013;34:1671–1673.
14. Tsivgoulis G, Zand R, Katsanos AH, Goyal N, Uchino K, Chang J, Dariotis E, Putaala J, Alexandrov AW, Malkoff MD, Alexandrov AV. Safety of intravenous thrombolysis in stroke mimics: prospective 5-year study and comprehensive meta-analysis. *Stroke*. 2015;46:1281–1287.
15. Grois D, Detlev M, Mulayoff A, Hadar O. Performance comparison of h.265/mpeg-hevc, vp9, and h.264/mpeg-avc encoders. Picture Coding Symposium, San Jose, CA, USA. December 8–11, 2013:394–397.
16. Marcus M, Pattan B. Millimeter wave propagation: spectrum management implications. *IEEE Microw Mag*. 2005;6:54–62.
17. Federal Communications Commission. 2018 Broadband deployment report. 2018. Available at: https://docs.fcc.gov/public/attachments/FCC-18-10A1.pdf. Accessed March 2, 2019.
18. Coutinho JM, Liebeskind DS, Slater LA, Nogueira RG, Clark W, Davalos A, Bonafe A, Jahan R, Fischer U, Gralla J, Saver JL, Pereira VM. Combined intravenous thrombolysis and thrombectomy vs thrombectomy alone for acute ischemic stroke: a pooled analysis of the SWIFT and STAR studies. *JAMA Neurol*. 2017;74:268–274.
19. Fitzgerald S. Is IV TPA needed with mechanical thrombectomy for stroke? *Neurol Today*. 2017;17:14.
20. Mandava P, Martini SR, Shah VA, Fabian RH, Kent TA. Abstract WMP1: Factors influencing differential outcomes in stent retriever trials: comparison to a new outcome model based on percent utilization of rt-PA. International Stroke Conference. Los Angeles, CA, USA. February 17, 2016. *Stroke*. 2016;47:AWMP1.

Key Words: Editorials • stroke • telemedicine • tissue-type plasminogen activator