

UC Irvine

UC Irvine Previously Published Works

Title

Increased Access to and Use of Endovascular Therapy Following Implementation of a 2-Tiered Regional Stroke System

Permalink

<https://escholarship.org/uc/item/8kg7j9j4>

Journal

Stroke, 51(3)

ISSN

0039-2499

Authors

Bosson, Nichole

Gausche-Hill, Marianne

Saver, Jeffrey L

et al.

Publication Date

2020-03-01

DOI

10.1161/strokeaha.119.027756

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

Increased Access to and Use of Endovascular Therapy Following Implementation of a 2-Tiered Regional Stroke System

Nichole Bosson, MD, MPH; Marianne Gausche-Hill, MD; Jeffrey L Saver, MD; Nerses Sanossian, MD; Richard Tadeo, RN; Christine Clare, RN; Lorrie Perez, RN; Michelle Williams, RN; Sara Rasnake, RN; Phuong-Lan Nguyen, MS; and the Los Angeles County Stroke Data Collaborative*

Background and Purpose—We quantified population access to endovascular-capable centers, timing, and rates of thrombectomy in Los Angeles County before and after implementing 2-tiered routing in a regional stroke system of care.

Methods—In 2018, the Los Angeles County Emergency Medical Services Agency implemented transport of patients with suspected large vessel occlusions identified by Los Angeles Motor Scale ≥ 4 directly to designated endovascular-capable centers. We calculated population access to a designated endovascular-capable center within 30 minutes comparing 2016, before 2-tiered system planning began, to 2018 after implementation. We analyzed data from stroke centers in the region from 1 year before and after implementation to delineate changes in rates and speed of administration of tPA (tissue-type plasminogen activator) and thrombectomy and frequency of interfacility transfer.

Results—With implementation of the 2-tier system, certified endovascular-capable hospitals increased from 4 to 19 centers, and within 30-minute access to endovascular care for the public in Los Angeles County, from 40% in 2016 to 93% in 2018. Comparing Emergency Medical Services–transported stroke patients in the first post-implementation year (N=3303) with those transported in the last pre-implementation year (N=3008), age, sex, and presenting deficit severity were similar. The frequency of thrombolytic therapy increased from 23.8% to 26.9% (odds ratio, 1.2 [95% CI, 1.05–1.3]; $P=0.006$), and median first medical contact by paramedic-to-needle time decreased by 3 minutes [95% CI, 0–5] $P=0.03$. The frequency of thrombectomy increased from 6.8% to 15.1% (odds ratio, 2.4 [95% CI, 2.0–2.9]; $P<0.0001$), although first medical contact-to-puncture time did not change significantly, median decrease of 8 minutes [95% CI, –4 to 20] $P=0.2$. The frequency of interfacility transfers declined from 3.2% to 1.0% (odds ratio, 0.3 [95% CI, 0.2–0.5]; $P<0.0001$).

Conclusions—After implementation of 2-tiered stroke routing in the most populous US county, thrombectomy access increased to 93% of the population, and the frequency of thrombectomy more than doubled, whereas interfacility transfers declined. (*Stroke*. 2020;51:908–913. DOI: 10.1161/STROKEAHA.119.027756.)

Key Words: Emergency Medical Services ■ neuron ■ odds ratio ■ reperfusion ■ thrombectomy

For patients with acute ischemic stroke, time is critical. In acute ischemic stroke due to large vessel occlusion (LVO), ≈ 2 million neurons die every minute that reperfusion is delayed.¹ Multiple randomized clinical trials have demonstrated benefit from endovascular thrombectomy for patients with anterior circulation LVO.^{2–6} However, the success of this treatment is dependent on early intervention. The sooner the thrombectomy is performed, the greater the benefit that is derived.^{7–11}

To reduce the time to intervention and increase thrombectomy for treatment of LVOs, several stroke expert consensus groups have recommended Emergency Medical Services (EMS) switch from single-tier routing, in which EMS transport all stroke patients to the closest stroke center, to 2-tiered routing, in which EMS transport the subset of stroke patients with suspected LVO directly to an endovascular-capable center, possibly bypassing primary stroke centers.^{12,13} Several observational studies have reported shorter time to intervention with direct transport compared with secondary transfer,

Received September 17, 2019; final revision received November 26, 2019; accepted January 2, 2020.

From the Department of Emergency Medicine, Harbor-UCLA Medical Center and The Lundquist Institute, Torrance, CA (N.B., M.G.-H.); Los Angeles County Emergency Medical Services Agency, Santa Fe Springs, CA (N.B., M.G.-H., R.T., C.C., L.P., M.W., S.R., P.L.-N.); David Geffen School of Medicine at UCLA, Los Angeles, CA (N.B., M.G.-H., J.L.S.); Ronald Reagan UCLA Medical Center, Los Angeles, CA (J.L.S.); and Keck University School of Medicine at USC, Los Angeles, CA (N.S.).

*A list of all Los Angeles County Stroke Data Collaborative members is given in the Appendix.

Guest Editor for this article was Seemant Chaturvedi, MD.

Presented in part at the International Stroke Conference, Honolulu, HI, February 6–8, 2019.

Correspondence to Nichole Bosson, MD, MPH, Los Angeles County EMS Agency, 10100 Pioneer Blvd Suite 200, Santa Fe Springs, CA 90670. Email nbosson@dhs.lacounty.gov

© 2020 American Heart Association, Inc.

Stroke is available at <https://www.ahajournals.org/journal/str>

DOI: 10.1161/STROKEAHA.119.027756

that is, drip-and-ship model.^{14–19} However, there is insufficient data regarding the effect of direct routing by EMS on patient outcomes.²⁰ Although researchers attempting to model single-tier routing versus 2-tier routing have suggested potential benefits to bypassing primary stroke centers for suspected LVOs, these models rely upon multiple assumptions and depend on the specific characteristics of the regional system.^{21,22} It is currently unknown whether moving from single-tiered to 2-tier routing will increase access to and frequency of thrombectomy treatment when actually implemented within a regional stroke system. There is also concern that bypassing closer hospitals could delay administration of tPA (tissue-type plasminogen activator), another time-sensitive intervention for stroke patients.^{19,23}

Los Angeles (LA) County transitioned from a single-tier to a 2-tier routing model in 2018. Taking advantage of this natural experiment, we quantified population access to endovascular-capable centers and frequency and timing of thrombolytic and thrombectomy therapy before and after system evolution.

Methods

This was a retrospective analysis of prospectively acquired registry data from the LA County EMS system. The study was reviewed and approved by the Harbor-UCLA Medical Center institutional review board. Data is available upon request from the LA County EMS Agency per LA County Reference 622: Release of EMS Data available at <http://dhs.lacounty.gov/wps/portal/dhs/ems/prehospitalcaremanual>.

LA County is a large metropolis, comprising 88 cities spanning over 4000 square miles with a population of ~10.2 million. LA County EMS Agency operates a regional stroke system of care. Patients with acute stroke who accessed 9-1-1 are transported by EMS to 1 of 51 Approved Stroke Center (ASCs). The LA County EMS Agency designates ASCs after certification by a Centers for Medicare and Medicaid Services–approved accrediting body, along with agreement by the hospital to provide 24/7 accessibility for EMS-transported stroke patients based on regional published standards.²⁴ All ASCs participate in a system quality improvement program, and 47 of the stroke centers submit data on patient treatment and outcomes to the Get With The Guidelines–Stroke registry, including all of the designated endovascular-capable centers.

During the study time period, paramedics screened patients with acute neurological symptoms with last known well time (LKWT) within 6 hours with the modified LA Prehospital Stroke Screen to identify patients with probable acute stroke. In addition, paramedics used clinical judgment regarding patients with LKWT within 6 hours who were modified LA Prehospital Stroke Screen negative with the ability to contact online medical control for direction if they continued to have a clinical suspicion for stroke. Paramedics routed all patients with suspected acute stroke and LKWT within 6 hours to an ASC. Patients with suspected acute stroke with LKWT >6 hours were routed to an ASC or to the closest non-ASC facility according to online medical control guidance; it was common for medical control to route all suspected acute strokes within 24 hours of LKWT to an ASC if reachable within 30 minutes. Beginning in 2016, paramedics utilized the LA Motor Scale (LAMS) to assess the stroke severity. However, paramedics continued to transport all patients with clinical suspicion of acute stroke and LKWT within 6 hours to the closest ASC, regardless of the LAMS.

On January 8, 2018, the LA County EMS Agency implemented a policy of 2-tiered routing such that patients with suspected

stroke with LKWT within 6 hours and LAMS 4 or 5 were routed to the closest designated endovascular-capable center (ie, thrombectomy-capable stroke center [TSC] or comprehensive stroke center [CSC]), if within a 30-minute transport time. Before this routing change, in 2016, the LA County EMS Agency initiated a process for designation of a second tier of stroke centers that had endovascular stroke capability. To be designated as an endovascular-capable center, ASCs were required to have been certified as a CSC or, as national certification for TSCs had not yet begun, were required to demonstrate current endovascular stroke capability on a site review by EMS staff (physician and nurse) and to achieve TSC certification from a Centers for Medicare and Medicaid Services–approved organization within the year. Patients with LAMS 0 to 3 continued to be routed to the closest ASC regardless of endovascular capabilities. Beginning in July 2018, patients with LAMS 4 to 5 and LKWT within 24 hours were routed to the closest endovascular-capable stroke center if reachable within 30 minutes.^{25,26}

For this study, we determined population access to a designated endovascular-capable center within 30 minutes using 2015 LA demographic data. We compared access in 2016, before system planning and designation of endovascular-capable centers began to 2018 after 2-tiered routing went into effect. In addition, we evaluated the frequency of tPA administration, thrombectomy, and interfacility transfer for higher-level care among patients with acute ischemic stroke using data from Get With The Guidelines–Stroke for 1 year before and after implementation of 2-tiered stroke

Table 1. Date of Certification or LA County Designation as an Endovascular-Capable Center

Approved Stroke Center	Date*
Ronald Reagan UCLA Medical Center	October 7, 2014
Cedars Sinai Medical Center	December 5, 2014
St. Jude Medical Center	February 2, 2015
Glendale Adventist Medical Center	August 14, 2015
Los Robles Hospital and Medical Center	October 18, 2016
Good Samaritan Hospital	December 14, 2016
Long Beach Memorial Medical Center	January 20, 2017
Huntington Hospital	June 20, 2017
PIH Health Hospital - Whittier	August 8, 2017
Kaiser Foundation Hospital - Los Angeles	August 11, 2017
Los Alamitos Medical Center	November 15, 2017
Methodist Hospital of Southern California	January 8, 2018
Providence Little Company of Mary Medical Center Torrance	January 8, 2018
Providence Saint Joseph Medical Center	January 8, 2018
Dignity Health Northridge Hospital Medical Center	February 5, 2018
Pomona Valley Hospital Medical Center	February 15, 2018
Torrance Memorial Medical Center	February 15, 2018
Providence Saint John's Health Center	March 1, 2018
Santa Monica UCLA Medical Center	May 1, 2018

PIH indicates Presbyterian Intercommunity Hospital; and UCLA, University of California Los Angeles.

*Date of Comprehensive Stroke Center certification is provided in advance of LA County designation. Hospitals certified before 2-tiered routing implementation were officially designated at the start of the 2-tiered routing program on January 8, 2018.

routing. Finally, we compared 5 process times before and after the routing change (1) time from paramedic on scene, that is, first medical contact, to emergency department arrival, that is, door; (2) time from first medical contact to start of intravenous lytic, that is, needle (FMCTN); (3) time from door to needle; (4) time from first medical contact to start of endovascular procedure, that is, puncture; and (5) time from door to puncture. For the latter comparisons, we included all adult patients with acute ischemic stroke transported to an ASC and included in Get With The Guidelines–Stroke registry during the study period. The pre-period was January 8, 2017 to January 7, 2018. The post-period was January 8, 2018 to January 7, 2019.

To calculate population access, we utilized the Create Drive-Time Area analysis on ArcGIS Online (Esri, Redlands, CA) to determine a 30-minute transport time radius around each endovascular-capable center. Esri uses historical traffic data from HERE, <https://www.HERE.com>. The 30-minute radius was determined based on typical conditions for Thursdays at 17:00, given this is the heaviest traffic time in LA County. We estimated the population geographic distribution from 2015 LA demographic data.²⁷ To compare the frequency of interventions before and after the policy change, data from Get With The Guidelines–Stroke were analyzed using SAS 9.4 (SAS Institute, Cary, NC) statistical software. We determined the frequency and calculated the odds ratios for tPA administration, thrombectomy, and interfacility transfer for higher-level care before and after the policy change. We calculated the medians with interquartile ranges for treatment time intervals for the pre-implementation and post-implementation periods and compared groups with the Hodges Lehmann median difference test.

Results

The announcement of planned implementation of 2-tiered routing was associated with an increase in the number of hospitals certified as endovascular-capable centers. At the start of 2016, the system had 4 CSCs and 45 Primary Stroke Centers (PSCs). At the end of 2018, the system had 17 CSCs, 2 TSCs, and 32 PSCs. The dates of certification or designation as an endovascular-capable stroke center for each ASC are shown in Table 1. In 2018, 93% of LA County's 10.2 million residents were within 30 minutes of an endovascular-capable center compared with 40% in 2016 (Figure).

Comparing EMS-transported stroke patients in 2018 post-implementation ($n=3303$) with those transported in 2017 pre-implementation ($n=3008$), baseline age, gender, and National Institutes of Health Stroke Scale were similar, though patients in the post-implementation period were slightly more likely to be non-Hispanic white (Table 2). In the pre-implementation period, 52% (1560/3008) of ischemic stroke patients were transported by EMS to one of the subsequently designated endovascular-capable centers; this increased to 68% (2232/3303) in the post-implementation period.

Administration of reperfusion therapies to EMS-transported patients increased concurrent with implementation of the 2-tier routing system. tPA administration among EMS-transported patients increased post-implementation as compared to the

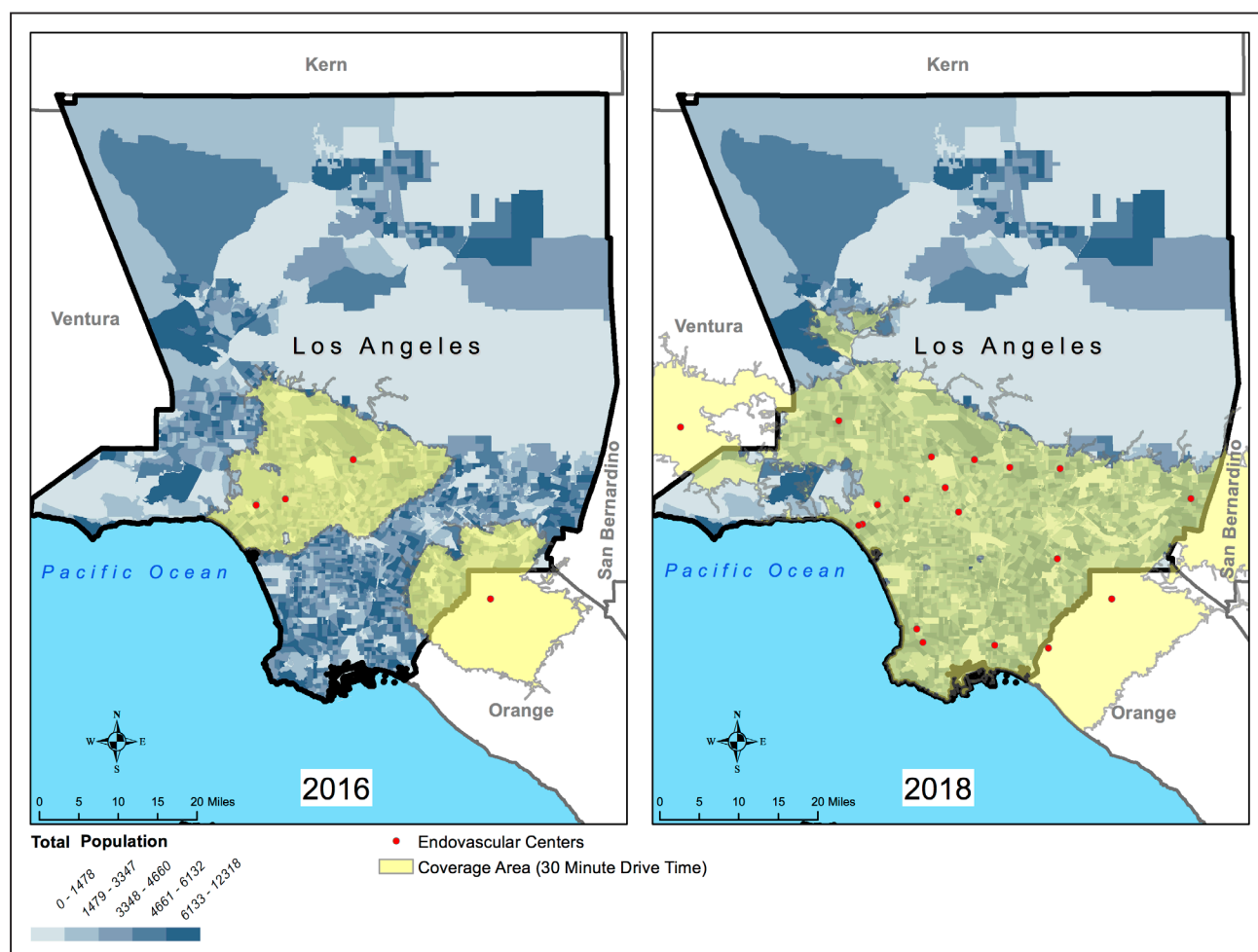


Figure. Access to endovascular-capable centers in Los Angeles County.

Table 2. Patient Characteristics by Routing Cohort

	Single-Tier (N=3008)		Two-Tier (N=3303)	
	N	%	N	%
Sex				
Male	1493	49.6	1566	47.4
Female	1513	50.3	1736	52.6
Unknown	2	0.1	1	0.0
Age, y, median/IQR	76	64–85	76	65–86
Race				
Asian	369	12.3	394	11.9
Black	374	12.4	402	12.2
White	1816	60.4	2127	64.4
American Indian	8	0.3	6	0.2
Pacific Islander	12	0.6	18	0.6
Mixed race	8	0.3	7	0.2
Unknown race	421	14.0	349	10.6
Hispanic ethnicity	733	24.4	696	21.1
NIHSS, median/IQR	7	3–16	7	3–17

IQR indicates interquartile range; and NIHSS, National Institutes of Health Stroke Scale.

pre-implementation period, 26.9% versus 23.8% (odds ratio, 1.2 [95% CI, 1.05–1.3]; $P=0.006$). Thrombectomy among EMS-transported patients increased substantially after the routing change, 15.1% versus 6.8% (odds ratio, 2.4 [95% CI, 2.0–2.9]; $P<0.0001$). The thrombectomy rates increased in each of the last known well to puncture time intervals of 0 to 6 hours, >6 to 8 hours, and >8 to 24 hours (Table 3). In addition, interfacility transfers for higher level of care significantly declined, 1.0% versus 3.2% (odds ratio, 0.3 [95% CI, 0.2–0.5]; $P<0.0001$).

There were no differences in first medical contact to emergency department door times between thrombectomy patients in the pre-implementation and post-implementation period, 26 minutes (interquartile range [IQR], 21–32) in both cohorts. Data were available for 99% of door to needle times and 93% of door to puncture times in both groups. Median door to needle time decreased in the post-implementation period, 45 minutes (IQR, 35–63) compared with 50 minutes (IQR, 38–66) pre-implementation, median decrease 4 minutes [95% CI, 2–6] $P=0.0006$. Door to puncture times did not change significantly. Median door to puncture time post-implementation was 104 minutes (IQR, 76–134) compared with 109 minutes (IQR, 82–149) pre-implementation, median change –7.5 minutes [95% CI, –16 to 1] $P=0.07$.

For paramedic on scene time to interventions, data were available for FMCTN time for 83% in the pre-period and 95% of the post-period and for first medical contact to puncture time for 71% of the pre-period and 90% in the post-period. Median FMCTN time decreased, from 76 minutes (IQR, 61–94) to 72 minutes (IQR, 59–91), median decrease 3 minutes [95% CI, 0–5] $P=0.03$. Median first medical contact to puncture time post-implementation was 129 minutes (IQR, 100–156)

Table 3. Frequency of Thrombectomy According to LKW to Puncture Time Interval by Cohort

Time Interval	Single-Tier (N=3008)		Two-Tier (N=3303)		Relative Change
	N	% of All	N	% of All	
All	204	100%	498	100%	↑ 144%
0–6 h	123	60%	304	61%	↑ 147%
>6–8 h	10	5%	19	4%	↑ 90%
>8–24 h	39	19%	89	18%	↑ 128%
>24 h	4	2%	3	1%	↓ 25%
Unknown	28	14%	83	17%	↑ 196%

LKW indicates last known well.

compared with 135 (IQR, 111–171) pre-implementation, median change –8 minutes [95% CI, –20 to 4] $P=0.2$).

Discussion

In this study, implementation of a 2-tiered routing policy in a large regional acute stroke care system was associated with a doubling of the population with 30-minute access to thrombectomy care to 93% of residents. The frequency of endovascular thrombectomy increased substantially from 1 in 15 to 1 in 7 EMS-transported ischemic stroke patients. The frequency of intravenous thrombolytic therapy also increased to a lesser degree. Interfacility transfer rates were reduced substantially from 1 in 31 EMS-transported patients to 1 in 100. Treatment time intervals were shorter or comparable, not longer, after 2-tier routing implementation, with time from paramedic on scene to start of intravenous lysis occurring 3 minutes faster in the post-implementation period.

In 2016, although over a year had passed since the first of the landmark trials demonstrating benefit from thrombectomy for LVO stroke, the regional acute stroke care system included only 3 certified endovascular-capable centers in county and one in a neighboring county, affording access to an endovascular-capable center within a 30-minute transport to just 40% of the LA County population. There was no designation process to distinguish these centers from other ASCs in the system. With the introduction of the system change to 2-tiered routing with endovascular-capable center designation, we found a large increase in centers seeking CSC or TSC certification. Stroke certification by a Centers for Medicare and Medicaid Services–approved accrediting body is a requirement for designation as an ASC in LA County. Hospitals must voluntarily seek these certifications, which take a substantial investment in resources. Additional resources are required to achieve a higher-level certification, so hospital leadership must recognize a benefit to this investment. EMS implementation of policies of direct routing to specialized centers can be a potent stimulus for hospitals to seek specialty service accreditation. Previously, in a study of California EMS systems, Schubert et al²⁸ found that initiation of 1-tier EMS routing of acute stroke patients to PSCs was associated with an increase in the number of facilities seeking this designation. In our later time period, it is likely that the anticipated further system change to 2-tier routing, with direct transport of select patients

to endovascular-capable centers, may have encouraged additional facilities to obtain endovascular-capable designation.

The potential to delay delivery of intravenous thrombolytic therapy with bypass of closer PSCs has been a concern for policies that route select patients directly to further endovascular-capable centers. The longer transport times could potentially increase FMCTN times or even reduced use of thrombolytics if prolonged transport causes patients to arrive at the hospital beyond treatment time windows. The data from our experience is reassuring; 2-tier routing was associated with both an increase in patients receiving thrombolytic therapy and reduced FMCTN time. Our findings are similar to prior studies that have found that faster door to needle times at CSCs compared with PSCs can offset longer transport times.^{19,29} Comparing treatment of acute ischemic stroke across the US between PSCs and CSCs, Man et al³⁰ found that CSCs had higher rates of tPA administration, and more patients were treated within 60 minutes from emergency department arrival. In our region, an additional factor mitigating potential delays in administration of tPA was the large number and wide geographic dispersion of hospitals with endovascular-capabilities and the policy limiting transport times for bypass at 30 minutes.

Another development in endovascular stroke care that occurred in the same time period as the implementation of the 2-tier routing system in LA County was wide adoption nationally of an expanded time window for thrombectomy, to include imaging-selected patients in the 6- to 24-hour time window. However, when comparing the frequency of thrombectomy before and after the routing change by time interval, we found that the increase occurred at least as strongly among patients treated within 6h of last known well, who were unaffected by the indication expansion. Therefore, altered patient selection was not the driving force behind the higher thrombectomy rates observed after 2-tier system implementation.

This study has limitations. First, with a longitudinal before-after design, this study is unable to determine causality. Specifically, temporal trends in thrombectomy as this new therapy is more widely adopted may have contributed to an increase in system-wide rates of thrombectomy even without 2-tiered routing. Other changes in practice during the study period may have contributed, in part, to the observed increases in treatment rates and decreases in treatment times. Second, as analyses were confined to primary 911 transports and not interfacility transfer patients, which may lead to a slight overestimation of the increase in thrombectomy and underestimate any decrease in thrombectomy treatment times between the 2 time periods if present. Third, these results are from a single urban-suburban EMS system may not be generalizable to other systems, particularly those in rural areas.

Summary

After implementation of 2-tiered stroke routing in the most populous US county, thrombectomy access increased to 93% of the population, and the frequency of thrombectomy more than doubled. The frequency of thrombolytic therapy also increased, whereas time to administration decreased. Further, interfacility transfers for higher levels of care declined.

Appendix

Los Angeles County Stroke Data Collaborative

Asif Taqui, MD, Los Robles Hospital and Medical Center; Cheryl Evans-Cobb, RN, Kaiser Foundation Hospital - Panorama City; Chris Clare, RN, Los Angeles County Emergency Medical Services Agency; Denise Gaffney, RN, Kaiser Foundation Hospital - Los Angeles; Gary Duckwiler, MD, Ronald Reagan UCLA Medical Center; Gautam Ganguly, MD, Beverly Hospital; Gene Sung, MD, Keck University School of Medicine at USC; Helaine Kaufman, RN, Providence Saint Joseph Medical Center; Ivan Rokos, MD, Olive View Medical Center; Jason Tarpley, MD, Providence Saint John's Health Center; Jeffrey Saver, MD, Ronald Reagan UCLA Medical Center; Jennifer Anotado, RN, Adventist Health White Memorial; Lorrie Perez, RN, Los Angeles County Emergency Medical Services Agency; Marianne Gausche-Hill, MD, Los Angeles County Emergency Medical Services Agency; May Nour, MD, Ronald Reagan UCLA Medical Center; Michelle Jocson, RN, Glendale Adventist Medical Center; Michelle Williams, RN, Los Angeles County Emergency Medical Services Agency; Nerses Sanossian, MD, Keck University School of Medicine at USC; Nichole Bosson, MD, MPH, Los Angeles County Emergency Medical Services Agency; Nima Ramezan, MD, Long Beach Memorial Medical Center; Nirav Patel, MD, Long Beach Memorial Medical Center; Patrick Lyden, MD, Cedars Sinai Medical Center; Reza Jahan, MD, Ronald Reagan UCLA Medical Center; Richard Tadeo, RN, Los Angeles County Emergency Medical Services Agency; Sara Rasnake, RN; Los Angeles County Emergency Medical Services Agency; Tamika Burrus, MD, Coast Plaza Hospital; William Mack, MD, Keck University School of Medicine at USC; Zahra Ajani, MD, Kaiser Foundation Hospital - Los Angeles

Disclosures

Drs Bosson and Gausche-Hill have no personal disclosures. Their institutions are affiliated with the University of California. The University of California Regents have patent rights in retrieval devices for stroke. Dr Saver's institution is owned by the University of California. The University of California has patent rights in retrieval devices for stroke. He has served as an unpaid site investigator in multicenter trials sponsored by Boehringer Ingelheim, Hoffman LaRoche, Medtronic, Stryker, and Neuravia, for which the UC Regents received payments on the basis of clinical trial contracts for the number of subjects enrolled. Dr Saver has received funding for services as a scientific consultant regarding rigorous trial design and conduct to Medtronic, Stryker, Cerenovus, and Boehringer Ingelheim (prevention only), and stock options for services as a scientific consultant regarding rigorous trial design and conduct to Rapid Medical. The other authors reports no conflicts. The Los Angeles County Stroke Data Collaborative conceived of the study. Drs Bosson, Gausche-Hill, Saver, and Sanossian designed the trial. C. Clare, L. Perez, M. Williams, S. Rasnake, R. Tadeo collected and prepared the data. Dr Bosson performed the quantitative analysis. Dr Nguyen performed the GIS (geographic information system) mapping. Dr Bosson drafted the article, and all authors contributed substantially to its revision.

References

1. Saver JL. Time is brain—quantified. *Stroke*. 2006;37:263–266. doi: 10.1161/01.STR.0000196957.55928.ab
2. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi: 10.1056/NEJMoa1411587
3. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792
4. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030. doi: 10.1056/NEJMoa1414905

5. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. doi: 10.1056/NEJMoa1503780
6. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al; SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285–2295. doi: 10.1056/NEJMoa1415061
7. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, et al; HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288. doi: 10.1001/jama.2016.13647
8. Khatri P, Yeatts SD, Mazighi M, Broderick JP, Liebeskind DS, Demchuk AM, et al; IMS III Trialists. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: an analysis of data from the Interventional Management of Stroke (IMS III) phase 3 trial. *Lancet Neurol*. 2014;13:567–574. doi: 10.1016/S1474-4422(14)70066-3
9. Goyal M, Jadhav AP, Bonafe A, Diener H, Mendes Pereira V, Levy E, et al; SWIFT PRIME Investigators. Analysis of workflow and time to treatment and the effects on outcome in Endovascular treatment of acute ischemic stroke: results from the SWIFT PRIME Randomized Controlled Trial. *Radiology*. 2016;279:888–897. doi: 10.1148/radiol.2016160204
10. Menon BK, Sajobi TT, Zhang Y, Rempel JL, Shuaib A, Thornton J, et al. Analysis of workflow and time to treatment on thrombectomy outcome in the endovascular treatment for small core and proximal occlusion ischemic stroke (ESCAPE) Randomized, Controlled Trial. *Circulation*. 2016;133:2279–2286. doi: 10.1161/CIRCULATIONAHA.115.019983
11. Jahan R, Saver JL, Schwamm LH, Fonarow GC, Liang L, Matsouka RA, et al. Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA*. 2019;322:252–263. doi: 10.1001/jama.2019.8286
12. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al; American Heart Association Stroke Council. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2018;49:e46–e110. doi: 10.1161/STR.0000000000000158
13. Pierot L, Jayaraman MV, Szikora I, Hirsch JA, Baxter B, Miyachi S, et al; Asian-Australian Federation of Interventional and Therapeutic Neuroradiology (AAFITN), Australian and New Zealand Society of Neuroradiology (ANZSNR), American Society of Neuroradiology (ASNR), Canadian Society of Neuroradiology (CSNR), European Society of Minimally Invasive Neurological Therapy (ESMINT), European Society of Neuroradiology (ESNR), European Stroke Organization (ESO), Japanese Society for NeuroEndovascular Therapy (JSNET), The French Society of Neuroradiology (SFNR), Ibero-Latin American Society of Diagnostic and Therapeutic Neuroradiology (SILAN), Society of NeuroInterventional Surgery (SNIS), Society of Vascular and Interventional Neurology (SVIN), World Stroke Organization (WSO), World Federation of Interventional Neuroradiology (WFITN). Standards of practice in acute ischemic stroke intervention: international recommendations. *J Neurointerv Surg*. 2018;10:1121–1126. doi: 10.1136/neurintsurg-2018-014287
14. Gerschenfeld G, Muresan IP, Blanc R, Obadia M, Abrivard M, Piotin M, et al. Two paradigms for endovascular thrombectomy after intravenous thrombolysis for acute ischemic stroke. *JAMA Neurol*. 2017;74:549–556. doi: 10.1001/jamaneurol.2016.5823
15. Perez de la Ossa N, Abilleira S, Dorado L, Urrea X, Ribo M, Cardona P, et al. Access to endovascular treatment in remote areas: analysis of the reperfusion treatment registry of catalonia. *Stroke*. 2016;47:1381–1384. doi: 10.1161/STROKEAHA.116.013069
16. Weber R, Reimann G, Weimar C, Winkler A, Berger K, Nordmeyer H, et al; Neurovascular Net Ruhr. Outcome and periprocedural time management in referred versus directly admitted stroke patients treated with thrombectomy. *Ther Adv Neurol Disord*. 2016;9:79–84. doi: 10.1177/1756285615617081
17. Hiyama N, Yoshimura S, Shirakawa M, Uchida K, Oki Y, Shindo S, et al. Safety and effectiveness of drip, ship, and retrieve paradigm for acute ischemic stroke: a single center experience. *Neurol Med Chir (Tokyo)*. 2016;56:731–736. doi: 10.2176/nmc.2016-0102
18. Park MS, Yoon W, Kim JT, Choi KH, Kang SH, Kim BC, et al. Drip, ship, and on-demand endovascular therapy for acute ischemic stroke. *PLoS One*. 2016;11:e0150668. doi: 10.1371/journal.pone.0150668
19. Froehler MT, Saver JL, Zaidat OO, Jahan R, Aziz-Sultan MA, Klucznik RP, et al; STRATIS Investigators. Interhospital transfer before thrombectomy is associated with delayed treatment and worse outcome in the STRATIS Registry (Systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke). *Circulation*. 2017;136:2311–2321. doi: 10.1161/CIRCULATIONAHA.117.028920
20. Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M, et al. European Stroke Organisation (ESO) - European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke [published online February 26, 2019]. *J Neurointerv Surg*. 2019. doi: 10.1136/neurintsurg-2018-014569. <https://jn.is.bmj.com/content/early/2019/02/28/neurintsurg-2018-014569.info>.
21. Holodinsky JK, Williamson TS, Demchuk AM, Zhao H, Zhu L, Francis MJ, et al. Modeling stroke patient transport for all patients with suspected large-vessel occlusion. *JAMA Neurol*. 2018;75:1477–1486. doi: 10.1001/jamaneurol.2018.2424
22. Ali A, Zachrisson KS, Eschenfeldt PC, Schwamm LH, Hur C. Optimization of prehospital triage of patients with suspected ischemic stroke. *Stroke*. 2018;49:2532–2535. doi: 10.1161/STROKEAHA.118.022041
23. Globler NK, Sporer KA, Guluma KZ, Serra JP, Barger JA, Brown JF, et al. Acute stroke: current evidence-based recommendations for prehospital care. *West J Emerg Med*. 2016;17:104–128. doi: 10.5811/westjem.2015.12.28995
24. Stroke Receiving Center Standards. County of Los Angeles Emergency Medical Services Agency. Available at: http://file.lacounty.gov/sdsinter/dhs/1016600_322-strokestandards20170109-signed.pdf. Accessed September 12, 2019.
25. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378:708–718. doi: 10.1056/NEJMoa1713973
26. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al; 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. doi: 10.1056/NEJMoa1706442
27. Hedderson J, Bixler J. *Los Angeles County GIS Data Portal 2015 Datasets*. Sacramento, CA: Los Angeles county Internal Services Department; 2016.
28. Schuberg S, Song S, Saver JL, Mack WJ, Cen SY, Sanossian N. Impact of emergency medical services stroke routing protocols on primary stroke center certification in California. *Stroke*. 2013;44:3584–3586. doi: 10.1161/STROKEAHA.113.000940
29. Lahr MM, Luijckx GJ, Vroomen PC, van der Zee DJ, Buskens E. Proportion of patients treated with thrombolysis in a centralized versus a decentralized acute stroke care setting. *Stroke*. 2012;43:1336–1340. doi: 10.1161/STROKEAHA.111.641795
30. Man S, Zhao X, Uchino K, Hussain MS, Smith EE, Bhatt DL, et al. Comparison of acute ischemic stroke care and outcomes between comprehensive stroke centers and primary stroke centers in the United States. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004512. doi: 10.1161/CIRCOUTCOMES.117.004512