



Published in final edited form as:

*Stroke*. 2018 May ; 49(5): 1217–1222. doi:10.1161/STROKEAHA.118.020620.

## Evolution Of A U.S. County System for Acute Comprehensive Stroke Care

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### Abstract

**Background and Purpose**—In Orange County, CA patients with suspected acute stroke are taken to stroke neurology receiving centers (SNRC) that are designated by County Emergency Medical Services (EMS) authorities as either hubs or spokes based on endovascular treatment (EVT) capability. We examined relationships between stroke details, reperfusion therapies, hospital transfers, and their change over time.

**Methods**—All patients from January 1, 2013 to December 31, 2015 for whom 911 was called within 7 hours of onset in whom EMS personnel suspected acute stroke were evaluated.

**Results**—Among 6,132 patients, 3,924 (64%) had confirmed diagnosis of stroke (74% ischemic/26% hemorrhagic), yielding diagnostic precision of 64% in the field. Of the 2,892 patients with acute ischemic stroke, acute reperfusion therapy was given to 29.2% (21.7% IV tPA

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#### Disclosures

Dr. Cramer has consulted for MicroTransponder, Roche, and Dart Neuroscience. Dr. Patel received speaker's bureau fees for Janssen Pharma.

only and 7.5 % EVT). Rates of EVT treatment of patients with ischemic stroke increased over time, more than doubling from 5.6% in 2013 to 12.5% (odds ratio per three-month quarter=1.09, 95% CI 1.04-1.14,  $p<0.0001$ ). Only 3.4% of patients with AIS were transferred from a spoke to a hub hospital, transfer rates were inversely related to age ( $p<0.0001$ ), and reperfusion therapy rates did not vary according to transfer status.

**Conclusions**—Favorable features of this acute stroke care system include reperfusion therapy in 29.2% of patients with ischemic stroke and substantial increases in EVT rates over time. Continued efforts to optimize acute stroke systems of care can be directed toward improving access to best acute stroke therapies.

### Keywords

Acute Stroke; System of Care; Large Vessel Occlusion; Reperfusion; Endovascular Therapy; Mortality; Demographics

## Introduction

Multiple recently published randomized controlled trials have demonstrated substantial benefit of endovascular treatment (EVT) in patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO)<sup>1-5</sup>. The results of these trials prompted a focused update in the AHA/ASA Guidelines for early management of AIS, establishing EVT as standard of care in selected patients, and recommending optimization of systems of care to facilitate delivery of this therapy<sup>6</sup>. In response to these updated Guidelines, we evaluated the existing system of acute stroke care in Orange County, CA, the 6<sup>th</sup> most populous county in the USA. This countywide system was established in 2009 with a key goal to maximize reperfusion therapies for AIS by defining stroke neurology receiving centers (SNRC) as spokes or hubs, with primary Emergency Medical Services (EMS) ambulance transport to centers with EVT capabilities (i.e., hubs). In this system, patients that present to spokes with AIS and suspected LVO are transferred by EMS to hubs for EVT. A detailed description and initial experience of this system has been previously published and soon after implementation included substantial rates of acute reperfusion therapies administration<sup>7</sup>.

The present report extends the prior work published by this consortium<sup>7</sup>, aiming to investigate the performance of this spoke-and-hub model with respect to stroke demographics, reperfusion therapies, hospital transfers, and their change over time since initial 2009 implementation. The main objective of our study was to identify potential areas of improvement with an ultimate goal to optimizing acute stroke triage and treatment for AIS due to LVO.

## Methods

In the state of California, individual counties administer emergency medical services separately. Orange County EMS regulates, monitors, plans, and coordinates pre-hospital emergency medical services, hospital emergency programs, trauma centers, and SNRC. This includes oversight of medical procedures and transport destination all 484 EMS ambulance units throughout the county. The current report examines data from all patients from the start

of 2013 to the end of 2015 for whom Orange County EMS was called via 911 within 7 hours (per EMS protocol) of onset for symptoms suggestive of possible stroke, and for whom EMS personnel suspected acute stroke at end of initial evaluation in the field. We conducted a retrospective review of these prospectively collected Orange County EMS data. The study protocol was approved by the UC Irvine Institutional Review Board, who waived the need for patient consent. The data that support the findings of this study are available in anonymous form from the corresponding author upon reasonable request and upon approval by Orange County Emergency Medical Services administration.

In the original SNRC operations system in Orange County, CA<sup>7</sup>, availability of interventional neurological endovascular services 24 hours/day, 7 days/week, was a preferred, but not required, resource to achieve designation as an SNRC hub. Since our prior report, at the start of 2014, all 9 SNRC hubs in this system became EVT-ready, although only three are Joint Commission certified as an Advanced Comprehensive Stroke Center. Subsequently, on April 1<sup>st</sup> 2015, Orange County EMS officially changed the SNRC criteria to require 24/7 neurointerventional capabilities for all hub centers, and extended the patients covered by this policy from five to seven hours from symptom onset.

EMS transported patients to a SNRC hub (1) as a suspected ischemic stroke if the patient was last seen normal in the past seven hours, no seizure occurred immediately before or upon arrival, Glasgow Coma Scale score >9, and new onset arm or face weakness was present; (2) as a suspected intracerebral hemorrhage if in the past seven hours a patient had sudden severe headache with at least one of vomiting, new neurological deficit (weakness, forced deviation of gaze, or asymmetric pupils), altered mental status, or marked hypertension (diastolic blood pressure >100 mm Hg); and (3) note that both diagnoses also required any blood glucose level <80 mg/dl to be corrected. A specific LVO scale was not used at the time of this study (although since data were collected for the current study, the Los Angeles Motor Scale has been adopted in this system). In this system, patients could be transferred for higher-level care. Transfers could occur when (1) a patient walked into a spoke hospital and was subsequently transported to a hub via EMS, (2) EMS took a patient to a spoke hospital, which then deemed higher-level care was needed, or (3) a hub hospital for whatever reason felt the transfer to another hub to be optimal. Transfer from a spoke to a hub was based on physician evaluation at the spoke after consulting with the responsible neurologist who was immediately available at a hub; here we relied on physician-physician evaluation and communication rather than a specific set of triage criteria. In rare instances, patients were explicitly transferred for insurance reasons, and these patients are not classified as transfers in current analyses.

For each patient triaged into the system by field EMS units, a standardized data collection sheet was completed and then submitted to Orange County EMS for inclusion into a central database. This data collection sheet was validated by Orange County EMS, as described previously<sup>7</sup>, using a standardized data dictionary, trained data entry personnel, and a data double entry system to develop the final database. Data conflicts that arose with double entry were reviewed and resolved as possible by the EMS Medical Director who had oversight responsibility for the database. In maintenance of the database, strict patient confidentiality (defined by the U.S. Health Insurance Portability and Accountability Act) was maintained.

At each hub SNRC, the stroke coordinator, who was trained in data recording by county EMS, completed the data form and forwarded it to the central EMS database.

### Statistical methods

Parametric statistical methods were used, as the normality assumption was valid for all measures using raw or transformed values. All analyses were two-tailed with  $\alpha=0.05$  and used JMP software (version 13.1, SAS Institute, Inc., Cary, NC). Logistical models included gender and age as covariates, and treated time as quarters (3-month blocks). In order to determine whether there was a change (transient or permanent) in EVT treatment rates following the time when pivotal trials demonstrating beneficial effects of EVT had been released<sup>1-5</sup> and AHA/ASA Guidelines were revised, an interrupted time series analysis repeated this logistical model adding a term indicating slope change around the second quarter of 2015.

## Results

### Patients studied

A total of 6,132 patients suspected of having stroke by EMS were transported to an SNRC hub or spoke from January 1, 2013 to December 31, 2015 and are included in the current analysis. Among these patients, 3,924 had a diagnosis of stroke confirmed at the SNRC, yielding a diagnostic precision of 64% in the field.

### Stroke subgroups

Among patients with a confirmed diagnosis of stroke, 2,892 (74%) were ischemic, among whom the median admitting NIHSS score (available in 2,805) was 6 [IQR 2-14], and 1,032 (26%) were hemorrhagic, among whom the median admitting Glasgow Coma Scale score (available in 809) was 14 [IQR 7-15]. Significant differences in clinical characteristics were found between these two subgroups (Table 1) with respect to age, ethnicity, and mortality: patients with hemorrhagic stroke were significantly younger; more likely to be Asian or Hispanic and less likely to be Caucasian; much more likely to die by discharge; and were more likely to be transferred to a hub as compared to those with ischemic stroke. The rate of inter-hospital transfer was lowest for non-stroke cases, which are a complex group populated by many different non-stroke diagnoses, only some of which warrant transfer for high-level care. The rate of inter-hospital transfer was highest for hemorrhagic strokes, which tend to be more severe and so are easier to recognize and more likely to require higher-level care.

### Acute reperfusion therapy

Among patients with AIS, 628 (21.7%) received IV tPA alone, 106 (3.7%) received EVT alone, and 111 (3.8%) received EVT combined with IV tPA, making a total of 29.2% of patients with ischemic stroke who received any acute reperfusion therapy. The rate with which IV tPA was administered did not change over time ( $p=0.82$ ). However, the rate with which EVT was provided (alone or in combination with IV tPA) did increase over time (Figure 1), more than doubling from the first quarter, during which 5.6% of patients with AIS received EVT, to the second quarter of 2015, when the figure peaked at 12.5%. Consistent with this, the main effect of time in the nominal logistic model was significant:

across each successive 3-month block of time, the odds ratio for receiving EVT was 1.09 (95% CI 1.04-1.14,  $p < 0.0001$ ). Adding baseline NIHSS score as a covariate had negligible effect on results, with the odds ratio for receiving EVT being 1.13 (95% CI 1.07-1.16,  $p < 0.0001$ ). Note too that the rate with which EVT was given increased substantially in 2015, spiking to a maximum value of 12.5% during the April-June quarter of that year (Figure 1).

An interrupted time series analysis further examined these temporal trends by assessing whether rates of EVT administration changed before vs. after the second quarter of 2015, the time when pivotal trials demonstrating beneficial EVT effects had been released<sup>1-5</sup> and AHA/ASA Guidelines were revised. A significant change in the rate of EVT administration was not found, whether looking for a transient peak ( $p = 0.053$ ) or a permanent change ( $p = 0.65$ ) in the slope of EVT administration over time.

### Inter-hospital transfer

Rates of inter-hospital transfer appear in Table 2. Differences were found between stroke subtypes. The rate of transfer was much higher ( $p < 0.0001$ , Table 1) among patients with hemorrhagic stroke (123/1,032, 11.9%) as compared to ischemic stroke (99/2,892, 3.4%). For patients in both the ischemic and the hemorrhagic groups, transfer was less likely in older patients and among Caucasians (Table 2). Also, mortality during the acute stroke admission did not differ according to transfer status for patients, for either stroke subtype.

Among only those patients with ischemic stroke, stroke severity (admitting NIHSS score) did not differ according to transfer status. Provision of acute reperfusion therapy also did not vary in relation to transfer status, whether considering IV tPA and EVT separately or together. Across all subjects, the rate of transfer increased over the three years, with the main effect of time being highly significant ( $p < 0.0001$ ). This was also true among only those patients with ischemic stroke ( $p = 0.008$ ).

### Discussion

We examined all 6,132 persons suspected of having a stroke that were transported by Orange County EMS over a three-year period. A total of 29.2% of the patients with ischemic stroke received acute reperfusion therapy, with rates of EVT but not IV tPA increasing over time. Inter-hospital transfers were significantly higher among patients with hemorrhagic as compared to ischemic stroke and increased over time, but transfers were not associated with differences in either acute mortality or reperfusion therapy administration rates.

In the population studied, 26% of confirmed strokes were hemorrhagic. This is twice the US rate of 13%<sup>8</sup>, a finding that may be attributable to the population demographics of Orange County, CA, where there is a relatively higher proportion of Asian (20.4%) and Hispanic (34.3%) persons<sup>9</sup>. In both of these populations, the risk of intracerebral hemorrhage may be increased<sup>10, 11</sup>. Patients with hemorrhagic stroke might also be so highly represented in the current EMS-transported cohort because this stroke subgroup is known to have greater ambulance use as compared to the subgroup of patients with ischemic stroke or TIA<sup>12</sup>. There was no difference with respect to stroke subtypes among Blacks, possibly due to the small sample size of this group in the current cohort. Hemorrhagic strokes were transferred

three-times more often than ischemic strokes (Table 1), possibly reflecting the complexity of the hemorrhagic stroke and that many of the SNRC hubs were not certified as Advanced Comprehensive Stroke Centers and thus may not have had sufficient resources available for the management of hemorrhagic strokes.

The rate of acute reperfusion therapy administration (29.2% of patients with acute ischemic stroke) in this system remained high and surpassed our value of 25.1% reported in 2012<sup>7</sup>. The IV tPA administration rate was high (25.4%), and the rate with which EVT (alone or combined with IV tPA) was given (7.5% of patients with ischemic stroke who called 911 within 7 hours of stroke onset) while substantial was lower than the IV tPA administration rate. On the one hand, it can be noted that this EVT treatment rate is much higher than the US average of 1.5% in 2015, a figure derived from the fact that 10,284 EVT were performed<sup>13</sup>, and assuming an annual stroke incidence of 795,000 of which 87% are ischemic<sup>8</sup>. On the other hand, the maximum achievable rate of EVT administration might be as high as 13<sup>14</sup>–20%<sup>15</sup>, and the currently reported rate of EVT administration can be increased. One means of achieving this might be improved recognition of LVO at earlier time points such as through prehospital scales specifically aiming to identify LVO<sup>16, 17</sup>, e.g., the Rapid Arterial Occlusion Evaluation (RACE) or Los Angeles Motor Scale (LAMS), or through neurophysiological methods such as rapid electroencephalography (EEG)<sup>18</sup>.

The rate with which EVT was administered increased significantly over the three-year period of this study (Figure 1), more than doubling from the first quarter of 2013 to the second quarter of 2015, when the figure reached a maximum of 12.5%. A key contributor to this temporal pattern is that, beginning in December 2014, a series of pivotal trials demonstrated beneficial effects of EVT<sup>1–5</sup>. This led to updated AHA/ASA Guidelines that concluded that systems of care should be organized to facilitate the delivery of this intervention<sup>6</sup>. Our findings mirror national trends in clinical practice that followed release of these data<sup>19</sup>. During the second quarter of 2015, Orange County EMS required all SNRC to become EVT-ready and extended the SNRC coverage time window for suspected stroke calling 911 from five to seven hours after symptom onset, aiming to reduce impact of transfer-related delays<sup>20,21</sup>. These policy changes were suggested to have influenced the observed peak EVT administration rates, however the interrupted time series analysis focused on the second quarter of 2015 did not support a causal relationship.

The rate with which patients were transferred increased over the three years, among all subjects ( $p < 0.0001$ ), and also among only patients with ischemic stroke ( $p = 0.008$ ). Likely, the rate of transfer could be increased further, e.g., by increased use of transfer criteria that have been recently developed for primary stroke centers<sup>22</sup>. However, the exact utility of transfers in the context of suspected LVO remains uncertain<sup>23</sup>. Older subjects and females with ischemic stroke were found to be transferred at a significantly reduced rate (Table 2), echoing findings from the GWTG Registry<sup>24</sup>, where differences in access, awareness, and stroke pathophysiology were suggested as contributory factors. Addressing these issues may be of direct clinical importance, for example, in light of the pronounced treatment effect of EVT for LVO in patients  $> 80$  years of age<sup>25</sup>. In the current cohort, EVT showed a non-significant increased rate of occurring more frequently among transferred patients (Table 2), which is likely complicated by the fact that small numbers of patients with ischemic stroke

were transferred over the three-year study period. Higher rates of transfer for patients with suspected LVO may be of particular benefit in specific scenarios, such as when transferring to a high volume center<sup>26</sup> or directly to a neuroangiography suite<sup>27</sup>.

Our report demonstrates evolving and improving a regional system of acute stroke care. There are several limitations to this study. First, patients beyond 7 hours of symptom onset were not captured, as per EMS protocols. This is based on the fact that historically, EVT has generally been performed within 6 hours of symptom onset. However, recent pivotal trials demonstrated substantial benefit of EVT in selected patients with anterior circulation LVO up to 24h after stroke onset<sup>28, 29</sup>. In light of these new data, the Orange County EMS triage protocol will be revised accordingly, incorporating clinical tools for diagnosis of LVO in the field in the extended 24 hour window. Second, information from SNRC hubs on LVO status and reperfusion treatment times was not available, limiting the granularity with which some analyses could be interpreted. Third, patients who arrived at an SNRC via their own transportation were also not captured. Fourth, the precision of an EMS diagnosis of stroke was 64%, but this figure would be better understood by additionally knowing the rate with which EMS incorrectly diagnosed stroke, information that is not available from the current database. Fourth, outcomes data are limited to in-hospital mortality. The results suggest opportunities to improve the process of stroke care delivery. The diagnostic precision of a stroke diagnosis by EMS personnel in the field might be improved by incorporating recent advances in pre-hospital assessment tools, including prehospital scales<sup>30</sup> and possibly EEG-based neurophysiological measures<sup>18</sup> as well. Other efforts to improve acute stroke care might focus on increasing stroke awareness among EMS personnel, optimizing inter-facility transport protocols, refining clinical criteria for vascular imaging in spoke centers, and eliminating gender- and age-related disparities.

## Acknowledgments

### Sources of Funding

This work received support from the NIH (K24HD074722).

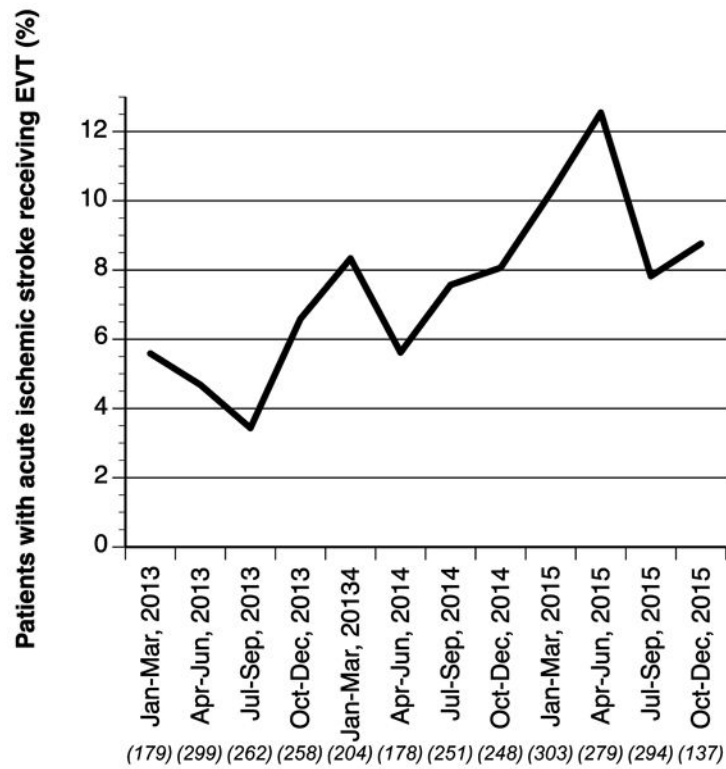
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**Figure 1.**

The percentage of patients with acute ischemic stroke receiving EVT (alone or in combination with IV tPA) increased over time ( $p < 0.0001$ ) and hit a peak in the second quarter of 2015. Numbers in parentheses are the total number of patients with acute ischemic stroke transported in a given 3-month quarter.

**Table 1**

Characteristics of patients with suspected acute stroke, according to diagnosis

	Ischemic	Hemorrhagic	Non-Stroke	p ischemic vs. hemorrhagic	p across all 3 groups
n	2,892	1,032	2,215		
Age	74.2 ± 14.4	66.0 ± 16.7	72.2 ± 15.9	<0.0001	<0.0001
Gender (%F)	52.7	49.5	54.6	0.078	0.025
Ethnicity					
Asian	10.4	17.6	8.0	<0.0001	<0.0001
Black	1.9	2.4	1.8	0.37	0.034
Caucasian	71.3	57.3	71.9	<0.0001	<0.0001
Hispanic	11.1	17.0	13.3	<0.0001	<0.0001
Other	5.4	5.8	5.1	0.63	0.0016
Died during acute hospital admission (%)	5.4	23.4	3.3	<0.0001	<0.0001
Transferred (%)	3.4	11.9	2.7	<0.0001	<0.0001

Values are percent, mean ± SD, or median [IQR]. Data are available in 6,121 subjects for age; 6,079, for gender; and 5,404 for mortality

**Table 2**

Characteristics of patients with acute stroke, according to transfer status

	Ischemic Stroke			Hemorrhagic Stroke		
	Transferred	Not Transferred	p	Transferred	Not Transferred	p
n	99 (3.4 %)	2,793 (96.6 %)		123 (11.9 %)	909 (88.1 %)	
Age	65.7 ± 15.3	74.5 ± 14.3	<0.0001	59.0 ± 17.6	67.0 ± 16.3	<0.0001
Gender (%F)	40.8	53.1	0.016	55.5	48.7	0.17
Ethnicity						
Asian	9.6	10.4	0.02	30.3	15.8	0.0005
Black	3.2	1.9	0.43	3.3	2.2	0.0001
Caucasian	58.5	71.7	0.003	41.8	59.4	0.52
Hispanic	17.0	10.9	0.09	15.6	17.1	0.001
Other	11.7	5.1	0.018	9.0	5.4	0.77
Died during acute hospital admission (%)	7.1	5.3	0.46	20.0	23.9	0.11
Baseline NIHSS score	6.5 [2.25-17]	6 [2-14]	0.39			0.34
Received IV tPA only (%)	22.2	21.7	0.90			
Received EVT (%) <sup>*</sup>	12.1	7.3	0.099			
Received any acute reperfusion therapy (%) <sup>^</sup>	34.3	29.0	0.26			

Values are percent, mean ± SD, or median [IQR]. Of the 2,892 patients with ischemic stroke, data for transfer status were available in 2,868; for baseline NIHSS, in 2,805.

<sup>\*</sup> with or without IV tPA.

<sup>^</sup> IV tPA, EVT, or both.