SUPPLEMENTAL MATERIAL

Impact of EMS bypass to endovascular capable hospitals: Geospatial modeling analysis of the US STRATIS Registry

SUPPLEMENTAL METHODS

Utilization of Google Maps Distance Matrix API

To calculate the travel distance and time from the stroke location to the ECC, a mapping application was developed using the Google Maps Distance Matrix Application Programming Interface (API). The "traffic model" parameter within the API was used to estimate the optimal travel times according to historical conditions and live traffic information. A database containing the geographic coordinates of the hospitals with stroke admissions and endovascular capabilities was linked to the application. To determine where strokes occurred, the nearest cross streets were identified in STRATIS and converted to geographic coordinates. Using the mapping application, the following information was entered to map several hypothetical bypass scenarios for each patient: 1) the geographic longitude and latitude coordinates of the field stroke location; 2) all hospitals within the same geographic range plus 5% (to allow for differential traffic flow); and 3) the next future time point matching the month, weekday, and the time of day of the stroke occurrence. The upcoming time point was selected to provide traffic conditions similar to those present at the time of stroke, as the Google API uses past traffic conditions to project upcoming conditions but does not provide direct access to individual time points in the past. To provide a best estimate of the traffic conditions at the time of each stroke event, a future date that corresponded to the actual date was entered in the API (e.g., if the stroke occurred on Wednesday, May 13, 2015 [week 20 of 2015], then Wednesday, May 16, 2018 [week 20 of 2018] was entered). Because the time that EMS departed from the incident location was not collected, arrival time at the incident location was used as the best estimate of departure time.

After the mapping application was run, a map showing the ECCs within the given distance from the stroke location was populated. For the first bypass scenario (direct transport to a STRATIS hospital), the STRATIS hospital was selected on the map, and the estimated travel time in traffic and travel distance from the stroke location was determined. For the aerial transport cohort, we compared actual air transport time "as the crow flies" compared to ground-based actual traffic prediction, following street detours. For the second bypass scenario (transport to the ideal hospital), the estimated travel time in traffic to several ECCs were determined; ultimately, the ECC with the shortest travel time was selected. When more than 1 hospital with the shortest estimated travel time was identified, the hospital with the shorter distance was selected.

Verification of the Mapping Application

To verify the data generated by Google Maps Distance Matrix API, the actual travel times, as reported by the sites in STRATIS, were compared with the calculated travel times. For the first validation the interval between recorded scene arrival time and nECC arrival was compared to the calculated time plus an assumed scene time of 15 minutes.[1-4] A recent US-based study using the National EMS Information Systems database to analyze 184,179 suspected stroke events reported a median on-scene time of 15 minutes, which were also published in the 2018 American Heart Association/American Stroke Association Guidelines.[2-4] The second validation compared the actual time interval between nECC departure and ECC arrival with the calculated time between nECC location and ECC location by the Google API.

Predictive Modeling

For modeled bypass transports, since data regarding EMS departure from stroke scenes was not collected, an on-scene time of 15 minutes was assumed to estimate scene departure times and time from scene departure to arrival at ECC door derived using the Google maps API. For IV-tPA-eligible patients, time from arrival at the ECC to thrombolytic treatment start was modeled using the mean actual door to needle time interval at the STRATIS ECC hospitals (37 minutes).[5] Outcomes for IV-tPA were modeled using the resulting onset to needle time. When the projected onset to needle exceeded 4.5 hours, outcomes were modeled assuming the patient would have proceeded directly to MT with prior IV-tPA. Time from arrival at the ECC to puncture was modeled using the mean actual door-to-puncture time at STRATIS ECC hospitals for direct-arriving patients (89 minutes).[6] For ecologic validity, all data used in modeling of clinical outcomes to assess the benefit of hypothetical bypass to ECC were derived from the STRATIS study, including the effect of time to needle (for patients receiving IV-tPA) and time to arterial puncture (for all patients irrespective of IV-tPA administration).

The effect of bypass on the distribution of mRS scores at 90 days was performed by comparing actual patient-level mRS with expected mRS under hypothetical bypass obtained from predictive modeling, with the models built using multilevel analysis in the following fashion (flowchart shown in Supplemental Figure 1 below):

1. Fields needed for prediction of outcomes were extracted from the database for all subjects in STRATIS, including mRS (the desired outcome variable), baseline characteristics, IV-tPA administration status, and workflow times.
2. Ordinal logistic regression models were then built from these overall data with mRS at 90 days as the outcome variable. Age, baseline NIHSS, and transfer mode (flight vs. ground) were included as covariates along with time from onset to IV-tPA administration and time from onset to groin puncture.
3. In parallel, time to IV-tPA administration (for those receiving IV-tPA) and time to arterial puncture were computed for each subject under hypothetical bypass using the Google API process (as previously described) to estimate workflow distances and times.
    a) Subjects found to be no longer eligible for IV-tPA based on increased time elapsed from stroke onset due to bypass were identified and noted.
4. For each individual subject, the ordinal logistic regression based on actual STRATIS data was then used to predict mRS outcomes under bypass, using separate models for patients receiving IV-tPA and those not receiving IV-tPA.
    a) To predict bypass outcomes, actual workflow times and tPA delivery status were replaced by modeled times and status under hypothetical bypass (derived from the API process cited above) and modeled mRS outcomes under bypass were thereby derived per-patient.
    b) Patients receiving IV-tPA in STRATIS but not expected to receive IV-tPA due to delays under hypothetical bypass were assessed using the non-IV-tPA model; these subjects were those identified in the preceding steps described here.
5. Modeled mRS outcomes under bypass were then aggregated and compared with actual outcomes from the same cohort of subjects to obtain summary results and statistical conclusions.

REFERENCES

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SUPPLEMENTAL TABLES

Table 1: Patient Demographic and Clinical Characteristics

Characteristic (n=236)	
Age (years)	66.4 ± 15.0
Male, n (%)	127 (53.8%)
Medical history, n (%)	
Atrial flutter/Atrial fibrillation	78 (33.1%)
Systemic Hypertension	173 (73.3%)
Diabetes mellitus	58 (24.6%)
Myocardial disease/Coronary artery disease	63 (26.7%)
Hyperlipidemia	107 (45.3%)
Peripheral artery disease	10 (4.2%)
Carotid artery disease	20 (8.5%)
Current or former tobacco use	115 (48.7%)
Pre-stroke mRS, n (%)	
0	181 (76.7%)
1	46 (19.5%)
2*	9 (3.8%)
NIHSS score	17.7 ± 5.5
ASPECTS (Core Lab)	7.8 ± 1.9
Occlusion Location, n (%)	
ICA	54 (22.9%)
M1	134 (56.8%)
M2	32 (13.6%)
Other	16 (6.8%)
Treatment with IV-tPA, n (%)	152 (64.4%)

mRS=Modified Rankin Scale; ICA=internal carotid artery; IV t-PA=intravenous tissue plasminogen activator; NIHSS=National Institutes of Health Stroke Scale; ASPECTS=Alberta Stroke Program Early CT Score

Supplementary Table II: Ground Cohort Distance and Time Intervals

Interval	Actual Mean ± SD (N) [median] (IQR)	Bypass to STRATIS hospital Mean ± SD (N) [median] (IQR)	p-value	Bypass to ideal hospital Mean ± SD (N) [median] (IQR)	p-
Distance: scene to initial hospital (mi)	8.1 ± 9.1 (115) [4.0] (2.0,11.0)	-	-	-	
Distance: initial to endovascular hospital (mi)	26.9 ± 25.2 (114) [17.0] (10.3,36.0)	-	-	-	
Distance: scene to endovascular hospital (mi)	-	31.7 ± 29.6 (117) [21.6] (13.7,37.1)	-	26.9 ± 26.1 (117) [18.6] (8.5,34.4)	
Onset to initial hospital	75.3 ± 58.5 (106) [54.5] (35.3,89.8)	-	-	-	
Onset to endovascular door	218.6 ± 80.0 (111) [210.0] (166.5,258.5)	109.0 ± 69.4 (117) [88.0] (62.0,141.0)	<0.001	102.2 ± 67.7 (117) [80.0] (52.0,124.0)	<0
Onset to IV-tPA	125.4 ± 52.2 (71) [111.0] (87.5,147.0)	135.9 ± 57.6 (73) [112.0] (95.0,169.0)	0.025	129.1 ± 55.5 (73) [108.0] (88.0,155.0)	0
Onset to arterial puncture	278.6 ± 83.1 (115) [265.0] (219.5,329.5)	198.6 ± 69.8 (115) [177.0] (151.5,231.5)	<0.001	191.8 ± 68.0 (115) [169.0] (141.0,213.5)	<0
EMS arrival to initial hospital	25.3 ± 10.9 (81) [23.0] (17.0,32.0)	-	-	-	
EMS arrival to endovascular door	170.2 ± 61.8 (109) [165.0] (133.0,194.0)	56.1 ± 30.2 (117) [46.0] (38.0,61.0)	<0.001	49.4 ± 26.5 (117) [41.0] (31.0,57.0)	<0
EMS arrival to IV-tPA	83.0 ± 28.8 (71) [78.0] (67.0,89.5)	93.3 ± 29.1 (73) [84.0] (75.0,98.0)	0.025	86.5 ± 25.3 (73) [80.0] (69.0,93.0)	0
EMS arrival to arterial puncture	225.1 ± 70.8 (115) [218.0] (183.0,255.0)	145.2 ± 30.4 (115) [135.0] (127.0,150.0)	<0.001	138.3 ± 26.6 (115) [130.0] (119.5,145.5)	<0

IV-tPA = intravenous tissue plasminogen activator; EMS = emergency medical services

Supplementary Table III: Aerial Cohort Distance and Time Intervals

Interval	Actual Mean ± SD (N) [median] (IQR)	Bypass to STRATIS hospital Mean ± SD (N) [median] (IQR)	p-value	Bypass to ideal hospital Mean ± SD (N) [median] (IQR)	p-value
Distance: scene to initial hospital (mi)	12.0 ± 16.3 (110) [7.0] (3.3,13.8)	-	-	-	-
Distance: initial to endovascular hospital (mi)	65.5 ± 46.5 (113) [56.0] (26.0,98.0)	-	-	-	-
Distance: scene to endovascular hospital (mi)	-	70.1 ± 46.4 (114) [60.2] (32.4,106.8)	-	56.9 ± 38.1 (114) [51.5] (24.5,83.9)	-
Onset to initial hospital	80.4 ± 60.9 (98) [60.5] (42.0,100.8)	-	-	-	-
Onset to endovascular door	239.8 ± 78.4 (110) [226.5] (175.0,295.8)	140.1 ± 66.0 (114) [131.5] (81.3,180.8)	<0.001	126.6 ± 61.8 (114) [114.5] (75.3,161.8)	<0.001
Onset to IV-tPA	124.8 ± 53.3 (73) [110.0] (85.0,153.0)	168.3 ± 62.2 (74) [161.0] (116.3,210.8)	<0.001	153.0 ± 56.3 (74) [141.5] (109.5,186.8)	<0.001
Onset to arterial puncture	295.8 ± 86.2 (112) [289.0] (225.8,351.0)	229.4 ± 66.5 (112) [220.5] (170.0,270.0)	<0.001	215.7 ± 62.3 (112) [203.5] (163.8,251.8)	<0.001
EMS arrival to initial hospital	32.5 ± 28.0 (68) [27.0] (21.8,34.0)	-	-	-	-
EMS arrival to endovascular door	193.1 ± 58.4 (110) [182.0] (151.0,225.0)	91.8 ± 43.6 (114) [81.5] (56.5,120.5)	<0.001	78.2 ± 36.2 (114) [68.5] (48.3,103.8)	<0.001
EMS arrival to IV-tPA	87.0 ± 38.7 (73) [77.0] (65.0,96.0)	130.9 ± 44.8 (74) [125.0] (95.3,155.5)	<0.001	115.6 ± 36.9 (74) [109.5] (86.3,136.0)	<0.001
EMS arrival to arterial puncture	247.2 ± 67.8 (112) [244.5] (194.8,285.5)	180.8 ± 44.0 (112) [170.0] (144.8,211.0)	<0.001	167.1 ± 36.5 (112) [155.0] (136.8,193.5)	<0.001

IV-tPA = intravenous tissue plasminogen activator; EMS = emergency medical services

SUPPLEMENTAL FIGURES

Supplementary Figure I. Geospatial route selection among nECCs and ECCs in relation to field location of stroke onset. In actual care, analyzed patients were first transported to the nearer non-endovascular capable center. In the bypass models, alternative routes evaluated were: A) direct transport to the STRATIS ECC, and B) direct transport to the iECC. This graph represents the models used in the analysis and does not reflect actual patient data.

Supplementary Figure II: Predictive model flow diagram.

Supplementary Figure III. Distribution of modeled scene to iECC distances. Histogram of modeled ground transport distances from field stroke scenes for the 117 patients with first transport to direct to STRATIS ECC, and with first transport to iECC. Bars indicate the proportions of patients within each distance interval. Data for the 53% of patients transferred by ground to iECC ≤20 miles are highlighted in green.

Supplementary Figure IV: Excess time from EMS scene arrival to IV-tPA start in patients bypassed ≤20 miles.

Supplementary Figure V: Modeled clinical outcomes for transport to ECC instead of nECC for any distance and within 20 miles.