**Online only Supplement**

PSC ELVO Transfer protocol

All patients underwent immediate NCCT and CTA as initial imaging at the PSC, confirming LVO and lack of a large completed infarct, and were subsequently transferred to the CSC with the intent to perform EVT. The transferring hospitals used a standardized transfer protocol, intended to reduce time to treatment. Key steps in this protocol included:

* Obtaining CTA upon arrival and immediately after NCCT in all cases, without waiting for serum creatinine
* Notifying the CSC upon arrival for patients with a LAMS of 4 or higher
* Mobilizing a transport team prior to CTA confirmation of ELVO
* Sharing images with the CSC through a secure, cloud based network (LifeImage). This allowed the CSC Neurointerventional team to review the CTA from the PSC prior to patient departure from the PSC.
* Transporting patients directly to the angiography suite upon CSC arrival without repeat imaging, unless there were prolonged transfer delays.

We began instructing PSCs on this protocol immediately after the results from the major randomized trials in 2015, and focused extensive efforts on education and implementation beginning July 1, 2015. By December 31, 2015, all PSCs had been instructed on these steps with in-person visits, and the electronic image sharing had been implemented. As such, we chose January 1, 2016 as the start period for our study.

Obtaining times from scene departure to hospital arrival.

In all patients, the time of first hospital arrival (PSC or CSC) was obtained from the electronic medical record. Additionally, as shown in Figure 1A, the exact field address of the EMS response was known in all except one patient. For 132 of the 242 patients closest to a PSC, exact EMS scene arrival and departure times were known. For the remainder, EMS scene departure time was back-calculated using the GoogleMaps API DriveTime function. The median difference between actual and calculated times for those patients with known scene departure times was 0.3 minutes. Additionally, the time and distance to the alternate hospital (i.e. the CSC in the Transfer group and the closest PSC in the Direct group) was calculated using the GoogleMaps API as well.

Matched Pairs Methodology

To attempt to control for baseline differences in time to CSC and stroke severity among all patients, we 1:1 matched Direct (case) with Transfer (control) by EMS time to CSC (+/- 5 minutes) and NIHSS (+/- 5) using the SAS macro %MATCH\_CC, resulting in 70 matched pairs (n=140). To control for possible pre-stroke mRS bias between groups, pre-stroke and 90-day mRS were nested within patient matches. Clinical outcome for the matched pairs was modeled in a similar fashion as for the entire cohort. To ensure that EMS time to CSC was controlled for, EMS scene to alteplase and arterial puncture were modeled as a function of time to CSC for the two groups using GLMM assuming a negative binomial distribution and nested by patient matches. For generalizability, we examined outcomes for all patients (to reflect actual clinical practice) and those with pre-stroke mRS <2 alone.

Supplemental Table1: Reason for triage to the PSC in the Transfer group (144 patients)

|  |  |
| --- | --- |
| Reason | Number |
| Patient in region without severity-based triage | 91 |
| Patient more than 30 minutes from CSC | 20 |
| Patient within 30 minutes from CSC, but field triage was not yet mandatory (before 3/1/2017) | 21 |
| Patient within 30 minutes from CSC, but taken to PSC for unknown reasons | 12 |
| TOTAL | 144 |

**Supplemental Figure 1: Graph of pre-stroke and 90 day mRs for all patients in the matched pairs cohorts.**

The graph of pre-stroke and 90 day mRs for the matched pairs (n=140) is below:



**Supplemental Figure 2: Rankin distributions in the Matched pairs model.**

All patients:



Independent at Baseline:



**Supplemental Table 2: Demographics and workflow outcomes presented as means (95% CI) for future meta-analyses.**

|  |  |  |  |
| --- | --- | --- | --- |
| All Patients | Transfer | Direct | p value |
| *Scene Geographic Information* |  |  |  |
| Drive time from scene to closest PSC (minutes) | 10.2 (9.3, 11.2) | 11.9 (10.6, 13.3) | 0.04 |
| Drive time from scene to CSC (minutes) | 30.3 (28.4, 32.4) | 18.7 (17.1, 20.5) | **<.001** |
| *EMS Scene workflow times (in minutes)* |  |  |  |
| Stroke onset to EMS arrival on scene | 130.2 (105.4, 160.9) | 184.7 (140.9, 242.0) | **0.05** |
| EMS on scene time | 15.9 (14.6, 17.2) | 13.7 (12.6, 14.9) | **0.01** |
| Scene departure to hospital arrival | 9.5 (8.7, 10.3) | 16.7 (15.1, 18.5) | **<.001** |
| *In-Hospital workflow times (in minutes)* |  |  |  |
| First Hospital arrival to alteplase | 62.0 (56.5, 68.2) | 40.6 (35.6, 46.3) | **<.001** |
| PSC arrival to departure (Door in to door out) | 94.2 (88.2, 100.6) | NA |  |
| Inter-facility Transport time | 25.2 (23.4, 27.1) | NA |  |
| CSC Arrival to arterial puncture | 36.9 (32.4, 42.0) | 92.1 (82.2, 103.2) | **<.001** |
| Arterial puncture to recanalization | 27.8 (25.0, 30.8) | 28.4 (25.2, 32.1) | 0.78 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | Transfer | | Direct | | *p* Value | |
| *Primary Workflow Outcomes (in minutes)* | |  | |  | |  | |
| All Patients | |  | |  | |  | |
| EMS Scene departure to alteplase | | 71.7 (66.0, 78.0) | | 57.5 (51.3, 64.5) | | **0.003** | |
| EMS Scene departure to arterial puncture | | 165.8 (154.9, 177.6) | | 108.9 (99.9, 118.8) | | **<.001** | |
| Matched Pairs | |  | |  | |  | |
| EMS Scene departure to alteplase | | 67.6 (59.4, 77.0) | | 60.1 (52.6, 68.8) | | 0.22 | |
| EMS Scene departure to arterial puncture | | 159.8 (143.5, 178.1) | | 112.4 (101.0, 125.1) | | **<.001** | |

**Supplemental Table 3:**

**Demographics for matched pairs model:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Transfer | Direct | P |
| Number | 70 | 70 |  |
| Age (median (Q1-Q3)) | 77 (66 - 84) | 77 (64 - 86) | 0.91 |
| Female No (%) | 38/70 (54%) | 36/70 (51%) | 0.73 |
| *Clinical Parameters* |  |  |  |
| NIHSS (median (Q1-Q3)) | 16 (12 - 22) | 17 (12 - 23) | 0.86 |
| IV tPA administered No (%) | 45/70 (64) | 39/70 (56) |  |
| Location of intracranial occlusion |  |  |  |
| Left hemisphere involved No(%) | 40/70 (57) | 33/70 (47) | 0.24 |
| ICA (No (%)) | 14/70 (20) | 8/70 (11) | 0.33 |
| M1 (No (%)) | 43/70 (61) | 50/70 (72) |
| M2 (No (%)) | 13/70 (19) | 12/70 (17) |
| NCCT ASPECTS (median (IQR)) | 10 (9 - 10) | 10 (9 - 10) | 0.39 |
| *Scene Geographic Information as median (Q1-Q3)* |  |  |  |
| Distance from scene to closest PSC in kma | 4.2 (2.2 - 7.5) | 8.2 (4.6 - 12.8) | **<.001** |
| Drive time from scene to closest PSC in minutes | 8.3 (5.1 – 1.6) | 12.4 (9.2 – 16.4) | **<.001** |
| Distance from scene to CSC in kma | 25.3 (17.1 - 32) | 20.6 (12.2 - 25.2) | **0.003** |
| Drive time from scene to CSC in minutes | 22.0 (17.3 – 26.3) | 20.5 (14.5 – 25.3) | 0.18 |
| *EMS Scene workflow times in minutes. Median (Q1-Q3)* |  |  |  |
| Stroke onset to EMS arrival on scene | 41.3 (15.2 – 138.0) | 64.0 (18.0 - 298) | 0.05 |
| EMS on scene time | 15.0 (11.5 – 19.0) | 14.0 (10.0 – 16.0) | 0.16 |
| Scene departure to hospital arrival | 7.6 (4.7 – 11.0) | 17.1 (13.0 – 21.0) | **<.001** |
| *In-Hospital workflow times in minutes. Median (Q1-Q3)* |  |  |  |
| First Hospital arrival to alteplase | 51.0 (36.0 – 72.0) | 33.0 (27.0 – 47.0) | **<.001** |
| PSC arrival to departure (Door in to door out) | 79.0 (64.0 – 106.0) | N/A |  |
| PSC arrival to CSC arrival | 18.0 (13.0 – 25.0) | N/A |  |
| CSC Arrival to arterial puncture | 21.0 (17.0 – 40.0) | 79.0 (54.0 – 102.0) | **<.001** |
| Arterial puncture to recanalization | 23.0 (14.0 – 33.0) | 25.0 (16.0 – 37.0) | 0.28 |
| First hospital arrival to arterial puncture | 128.0 (103.0 – 183.0) | 79.0 (54.0 – 102.0) | **<.001** |
| First Hospital arrival to Recanalization | 158.0 (125.0 – 216.0) | 112.0 (80.0 – 135.0) | **<.001** |
| *Angiographic Reperfusion No. (%)* |  |  |  |
| Successful recanalization (mTICI 2b or better)b | 49/61 (80) | 59/67 (88) | 0.44 |
| mTICI 0/1 | 5/61 (8) | 2/67 (3) |  |
| mTICI 2a | 7/61 (12) | 6/67 (9) |  |
| mTICI 2b | 13/61 (21) | 20/67 (30) |  |
| mTICI 2c/3 | 36/61 (59) | 39/67 (58) |  |

a To convert km to miles, divide by 1.6

bAmong those who underwent EVT. mTICI = Modified Thrombolysis in Cererbal Infarctio

**Supplemental Table 4: Sensitivity analysis: Primary workflow and clinical outcomes in sensitivity analysis. Assumes all patients in the Direct group who were lost to follow-up (n=3) were dead at 90 days and that all patients in the Transfer group who were lost to follow-up (n=7) were at their pre-stroke mRs at 90 days.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | Transfer | Direct |  | *p* Value |
| *Primary Workflow Outcomes (in minutes), median (Q1-Q3)* | | | | |  |
| All Patients | |  |  |  |  |
| EMS Scene departure to alteplase | | 64 (49.5 – 86) | 50 (42 – 63) |  | **<.001** |
| EMS Scene departure to arterial puncture | | 152 (116.5 - 194) | 93 (67 - 125) |  | **<.001** |
| *Primary Clinical Outcomes (with assumptions as above)* | | | | |  |
|  |  | Modifed Rankin Score at 90 days mean (95% CI) | | Odds Ratio (95% CI) for less disability |  |
| All patients | | 3.2 (3.0 – 3.4) | 3.0 (2.7 – 3.2) | 1.2 (1.0 – 1.5) | .0597 |
| All patients (independent pre-stroke) | | 2.7 (2.4 – 2.9) | 2.2 (1.9 - 2.5) | 1.4 (1.0 – 1.8) | **.0137** |