

Prehospital and Emergency Department-Focused Mission Protocol Improves Thrombolysis Metrics for Suspected Acute Stroke Patients

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Background: The Mission Protocol was implemented in 2017 to expedite stroke evaluation and reduce door-to-needle (DTN) times at Zuckerberg San Francisco General Hospital. The key system changes were team-based evaluation of suspected stroke patients at ambulance entrance by an Emergency Department (ED) physician, ED nurse, and neurologist and immediate emergency medical service (EMS) provider transport of patients to CT. *Methods:* Patients were eligible for a Mission Protocol prehospital stroke activation if an EMS provider found a positive Cincinnati Prehospital Stroke Scale and a last known normal time within 6 hours. We retrospectively compared treatment metrics between the first year of Mission Protocol patients and patients from the year prior also brought in via ambulance with suspected stroke and a last known normal time within 6 hours. Median Door to CT and DTN times were compared using 2 sample Wilcoxon rank-sum (Mann-Whitney) tests. *Results:* There were 236 patients in the Mission Protocol group and 112 in the comparison group. The Mission Protocol was associated with a 10 minutes faster median door to CT time ($P < .00001$), a 6 minutes faster median DTN time ($P = .0046$), a 22% increase in the proportion of patients treated within 45 minutes of arrival (84% versus 62%), and a 12% increase in the proportion of patients treated within 60 minutes (92% versus 80%). There were 8 stroke mimics treated in the Mission Protocol cohort compared to 2 in the comparison cohort. Symptomatic intracranial hemorrhage occurred in one Mission Protocol patient with an ischemic stroke. *Conclusions:* The EMS direct to CT based Mission Protocol was associated with faster median door to CT and DTN times. There was a 22% increase in the proportion of thrombolysis patients treated within 45 minutes or less. More stroke mimic patients received thrombolysis but symptomatic intracranial hemorrhage only occurred in 1 ischemic stroke patient.

Key Words: Stroke—ischemic stroke—prehospital—emergency medical service
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Introduction

Ischemic stroke affects 17 million people and is the second most common cause of death worldwide each year.¹

It is the leading cause of disability in the United States.² For every minute a large cerebral vessel is occluded, approximately 1.9 million neurons are lost.³ This is the basis of the “time is brain” concept. Thrombolysis with

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intravenous tissue plasminogen activator (IV-tPA) is a proven, effective treatment^{4,5}; however, the benefits of thrombolysis are time dependent.⁶ As a result, there has been immense focus on improvement initiatives to reduce the time from hospital arrival to IV-tPA administration, which is referred to as the “door to needle time.”^{7,8}

The American Heart Association/American Stroke Association Target: Stroke Phase II initiative was implemented in 2014 to help participating hospitals improve door to needle (DTN) times.⁹ Best practice strategies were identified and all Get With the Guidelines – Stroke (GWTG-Stroke) hospitals⁹ were invited to participate. The primary goal of Target: Stroke Phase II was for hospitals to achieve DTN times within 60 minutes in at least 75% of patients treated with IV-tPA and DTN times within 45 minutes in at least 50% of patients.⁹ After implementation, GWTG-Stroke hospitals reported using a majority of the improvement strategies except for emergency medical services (EMS) transport of patients directly to CT/MRI scanner, premixture of IV-tPA ahead of time, initiation of IV-tPA in the imaging suite, and prompt feedback to EMS providers.⁹

In July of 2017, Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG) implemented a team-based approach to stroke care from EMS to CT scanner called “Mission Protocol” in the Emergency Department (ED). A Mission Protocol code stroke was activated prior to the patient’s arrival whenever an ED registered nurse received an EMS prehospital notification for a patient being brought to ZSFG with an impression of suspected stroke, a positive Cincinnati Prehospital Stroke Scale (CPSS), and a last known well time within 6 hours. With a Mission Protocol activation, an ED nurse, ED physician, and neurologist assembled at the ambulance entrance to perform a rapid, team-based evaluation of the patient. Mission Protocol included the least utilized GWTG-Stroke improvement strategies mentioned above and emphasized EMS feedback.

We sought to assess whether these strategies increased the percentage of patients treated with IV-tPA with a DTN time within 45 minutes. To accomplish this, we performed a retrospective cross-sectional study of the ZSFG ED stroke registry comparing process metrics between Mission Protocol patients and patients from a comparison subset of ED suspected stroke patients from the year prior.

Methods

Process Change

With a Mission Protocol activation, an ED nurse, ED physician, and neurologist assembled at a designated drop off location near the ambulance bay prior to patient arrival. This location, coined, “Mission Drop-off” included a gurney scale, computer, and a basic IV cart with a portable cardiac monitor. The ED nurse, ED physician, and neurologist were present for handoff, including vital signs and fingerstick glucose level, from the paramedic. At Mission Drop-off, the ED physician screened for potential life threats and ruled out rapidly

apparent stroke mimics while the neurologist confirmed ongoing suspected stroke and assessed for IV-tPA contraindications. During this evaluation, the ED nurse drew blood from an established prehospital IV line. It was under the decision of the ED physician whether the patient should proceed to CT scanner or go to a resuscitation room either for stabilization or further work-up of nonstroke etiology of symptoms. The ED physician placed orders for stroke imaging. After rapid evaluation at Mission Drop-off, the patient was weighed on the gurney scale prior to CT scan. The first transfer of patient was from ambulance gurney directly to CT scanner table. Once on the CT scanner table, the paramedic weighed the gurney on the scale in order to calculate the patient’s weight, and aid with medication (i.e., IV-tPA) dosing. The paramedics were asked to stay in the CT control room through completion of the CT scan in order to debrief the case. Based on the CT scan, IV-tPA was administered to the patient directly on the CT scanner table while a second IV line was established by the ED nurse. During IV-tPA infusion, the CT angiogram and perfusion scans were obtained. Mission Protocol was an adaptation of the Helsinki method¹⁰ with an enhanced focus on prehospital and ED involvement.

Prior to Mission Protocol implementation, potential stroke patients were roomed in the Emergency Department after which an EMS to ED physician sign out occurred. The ED physician evaluated the patient, activated a “code stroke,” in order for the patient to then be evaluated by a neurologist, transferred from ED room to CT scanner, and then subsequently weighed if eligible for IV-tPA. Although IV-tPA was administered on the CT scanner table prior to Mission Protocol implementation, this was sometimes given after CT angiogram and perfusion and there was not a specific protocol outlining the sequence of events including establishing second IV line and administering IV-tPA prior to further CT scans. The process for activating endovascular therapy (EVT) for patients was unchanged.

Besides process change in the hospital, the most profound changes were in the education and feedback provided for paramedics. This was accomplished through several means including both an educational training seminar and educational video open to all paramedics of San Francisco on Mission Protocol and an update on stroke care including LVO management. The on-site training session was attended by approximately 15% of paramedics in San Francisco. The educational video was available to all EMS personnel for viewing. Each individual stroke case was debriefed in real time during stroke cases with the paramedics and posters outlining the diagnoses and outcomes of patients were sent to corresponding ambulance agencies. Mission Protocol system changes and educational efforts are highlighted in [Table 1](#).

Selection of Participants

Consecutive Mission Protocol patients presenting between July 2017 and July 2018 were included in this study. ED

Table 1. Mission protocol system changes and educational efforts

<i>System changes</i>
<ul style="list-style-type: none"> • Prehospital stroke activation for patients with a positive Cincinnati Prehospital Stroke Scale and a last known well time within 6 h • Mission Protocol team (ED nurse, ED physician, and neurologist) assembled at ambulance entrance upon patient arrival • First patient transfer is from EMS gurney to CT scanner • EMS gurney weighed with patient on way to CT and weighed again after patient dropped off to determine IV-tPA weight • Premixture of IV-tPA at CT scanner and resupply of Stroke Kit
<i>Educational efforts</i>
<ul style="list-style-type: none"> • Free online Mission Protocol training video for EMS providers • Free EMS stroke education event where the protocol was reviewed • Direct, prompt EMS feedback during stroke cases • EMS feedback posters sent to ambulance agencies outlining outcome of individual stroke cases

Abbreviations: CT, computed tomography; ED, emergency department; EMS, emergency medical service; IV-tPA, intravenous tissue plasminogen activator.

suspected stroke patients that did not meet Mission Protocol criteria during this time period had standard code stroke activations and were not included in this study. Patients from the year prior to the implementation of the Mission Protocol were included for comparison if they were brought to ZSFG by ambulance from July 2016 to June 2017 with concern for stroke at the initial ED triage and an ED physician or registered nurse documented a last known well time within 6 hours of arrival. At the time of our study, San Francisco EMS policies already required that suspected stroke patients be brought to the nearest stroke center. Prehospital suspected stroke patients brought to hospitals other than ZSFG were not available for study. Only patients transferred directly to our ED were included. There were no transfer patients included in this study. All patients were included in the cohort and no outliers were excluded as has been in other stroke process studies.¹¹

Data

The data were abstracted by medical students and scribes via retrospective chart review. Data abstractors were all trained and all data were reviewed by the primary author (DYM). The primary predictor variable was membership in either the thrombolysis group from the year prior to implementation of the Mission protocol, termed “Year Prior,” or membership in the “Mission Protocol” group. The University of California, San Francisco Institutional Review Board approved our study.

Outcomes Measured

The primary outcome was the rate of DTN times of 45 minutes or less. Door time was time of patient arrival to the ED. Secondary outcomes included the median time from arrival to CT scan acquisition (door to CT time), median DTN times, the rates of patients with DTNs of 60

minutes or less, stroke mimic status at final diagnosis, and symptomatic intracranial hemorrhage (sICH). Median arrival to arterial puncture times for patients undergoing EVT, or “door to groin” (DTG) times, were also compared among all patient from these groups who had thrombectomies regardless of whether or not they received intravenous thrombolysis. Discharge diagnoses (stroke mimic or not) and sICH were retrospectively determined for each patient after chart and imaging review by a vascular neurology trained fellow (KJK). Symptomatic ICH was defined according to ECASS II criteria of hemorrhage on imaging and documentation of clinical deterioration or worsening of the National Institutes of Health Stroke Scale by 4 or more points.¹² Blinding to whether the patient was in the pre-Mission Protocol or post-Mission Protocol group was not possible within our chart review system.

Statistical Analysis

Medians of variables with skewed distributions such as age, baseline National Institutes of Health Stroke Scale, DTN, door to CT, and DTG times were compared using Wilcoxon rank sum tests. Comparisons of dichotomous variables between the Year Prior and Mission Protocol thrombolysis groups were made using Chi-squared tests. We considered *P* values less than .05 as statistically significant. All tests were 2-sided. STATA 15 (College Station, TX) was used for all analyses.

Results

Of the 112 patients in the Year Prior emergency department stroke registry, 45 were given IV-tPA and included in this analysis. Of the 236 Mission Protocol patients, 50 were given IV-tPA and included in this analysis. Table 2 describes the baseline demographic and baseline characteristics of thrombolysis patients in each group. There were no statistically significant differences between groups. History of coronary artery disease and tobacco use were not available in our data.

Table 3 compares various thrombolysis metrics between the Year Prior and Mission Protocol groups. The rate of door DTN times less than or equal to 45 minutes, our primary outcome, was 62% in the Year Prior and 84% in the Mission Protocol group (*P* = .02). There was a 10-minute improvement in median door to CT times (19 versus 9 minutes, *P* < .01) and a 6-minute improvement in median DTN times (35 versus 29 minutes, *P* < .01). Fig 1 provides a box plot representation of the changes in door to CT and DTN times between the 2 groups. The rate of patients with DTN times of less than or equal to 60 minutes was 12% higher in the Mission Protocol group though this change was not statistically significant (80% versus 92%, *P* = .09). Similarly, more mimic patients were treated with thrombolysis in the Mission Protocol group (2 versus 8, *P* = .07) though this difference was not statistically

Table 2. Demographic and baseline characteristics of thrombolysis patients

	Year prior (N = 45)	Mission protocol (N = 50)	P value
Age, y median (IQR)	70 (62-82)	71 (61-81)	.81
Female sex, %	49	52	.76
Race/ethnicity			
White non-Hispanic, %	20	22	.81
Black, %	36	18	.52
Hispanic, %	20	26	.49
Asian, %	20	32	.19
Unknown or declined to specify, %	4	2	.50
Baseline NIHSS, median (IQR)	8 (5-13)	10 (6-16)	.13
Prior stroke, %	36	30	.56
Hypertension, %	82	72	.24
Diabetes mellitus, %	27	30	.72
Atrial fibrillation, %	24	16	.30
Hyperlipidemia, %	42	40	.83
Housed, %	93	96	.58
English Language, %	73	68	.57
Intubated, %	4	2	.50

Note: A single baseline NIHSS for the Year Prior group was not documented.

Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

Table 3. Thrombolysis metrics between year prior and mission protocol groups

	Year prior (N = 45)	Mission protocol (N = 50)	P value
DTN time \leq 45 min, %	62	84	.02
Door to CT in minutes, median (IQR)	19 (14-23)	9 (5-11)	<.01
DTN time in minutes, median (IQR)	35 (32-57)	29 (22-36)	<.01
Min DTN in minutes	16	14	–
Max DTN in minutes	132	116	–
DTN time \leq 60 min, %	80	92	.09
Mimics treated, n (%)	2 (4.4)	8 (16)	.07
sICH, n (%)	0 (0)	1 (2)	.34

Abbreviations: DTN, door to needle; IQR, interquartile range; sICH, symptomatic intracranial hemorrhage.

significant. There was only 1 sICH in the Mission Protocol group and no sICH in the Year Prior group ($P = .34$).

Among all 348 patients studied, 14 patients in the Year Prior group and 22 patients in the Mission Protocol group underwent attempted thrombectomy. One patient from the Mission Protocol group was excluded from this analysis because they initially improved back to near baseline and thrombectomy was only performed after a decompensation

hours later attributed to residual clot propagation. Median DTG artery puncture times were 108 minutes (IQR 84-171) in the Year Prior group and 103 minutes (IQR 88-126) in the Mission Protocol group ($P = .61$).

Discussion

Evidence-based guidelines have reflected the time-dependency of IV-tPA efficacy by establishing more stringent DTN time goals.⁷ Involving EMS in improvement programs through advance notification of patient arrival^{13,14} and direct EMS-to-CT scanner transfer^{10,15} leads to faster door-to-imaging and DTN times, along with increased stroke reperfusion rates. Mission Protocol differs from prior documented improvement strategies in that it is ED led and managed. The ED physician rules out potential life threats and determines stability for CT scan. This is different from prior studies examining a neurologist at ambulance entrance to confirm stroke prior to direct EMS transfer to CT scanner table¹⁰ and also differs from newer studies examining a direct to EVT strategy being implemented at endovascular centers.¹⁶ This process was intentionally different from prior adaptations of the Helsinki method¹⁰ in that the focus was on ruling out potential stroke confounders prior to transfer to CT and enhanced paramedic engagement.

By implementing an ED and prehospital-focused approach to stroke care, we were able to meet the AHA/ASA goal of increasing the percentage of patients with DTN less than or equal to 45 minutes from 62% to 84% over the course of 1 year. Our DTN times before and after our intervention decreased from a median of 35 to 29 minutes. Our site is an urban, academic, stroke center with stroke center certification for 10 years and ongoing improvement processes that have led to a significant proportion of DTN times less than or equal to 60 minutes prior to the intervention. As a result, it is possible that this intervention had only a 6-minute decrease in median DTN times due to a "floor effect." The focus of this intervention was to increase the proportion of patients achieving a DTN time less than or equal to 45 minutes. We anticipate greater benefits of the Mission Protocol intervention in systems with baseline higher DTN times.

The major difference between Mission Protocol and other direct EMS-to-CT scanner transfer protocols is that Mission Protocol implemented a team of providers, including an ED nurse, ED physician, and neurologist, to meet suspected stroke patients and paramedics at the ambulance entrance and that Mission Protocol emphasized paramedic feedback and education. We were unable to identify other studies examining a team-based approach to a direct EMS-to-CT scanner method. This increased our efficiency in treating stroke. Immediate ED Physician and nursing assessments also ensured that unstable patients were identified and diverted to a resuscitation room for stabilization prior to CT. Threlkeld et al found that, at our institution, 11 individual

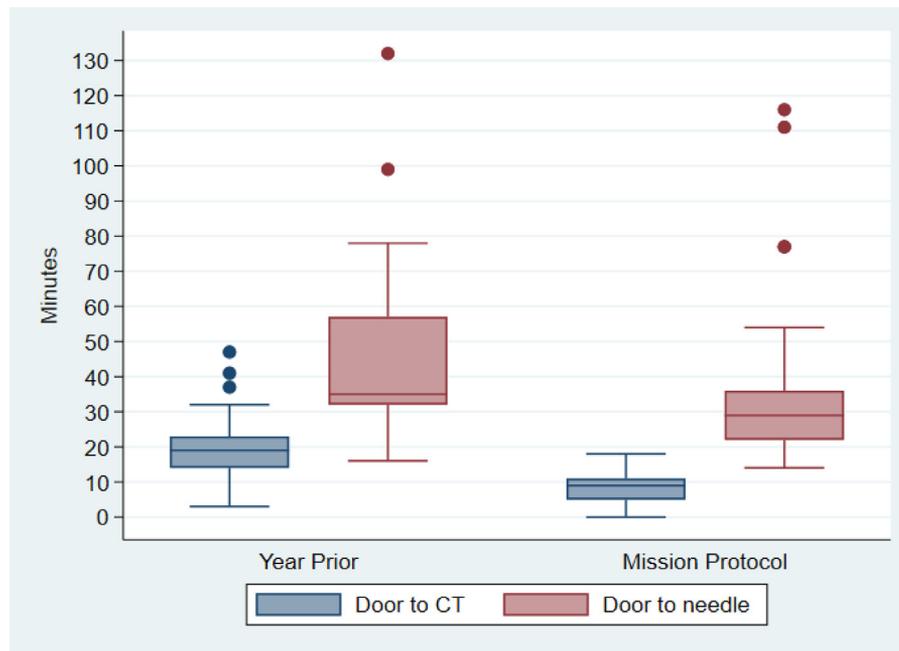


Figure 1. Comparison of door to CT and door to needle times between year prior and mission protocol groups. The blue box plot represents door to CT times and the red box plot represents door to needle times in both year prior and mission protocol. DTN and door to CT times for mission protocol are lowered compared to times in year prior. (Color version of figure is available online.)

improvement interventions initiated from 2011 to 2014 improved median DTN from 87 to 49 minutes.¹⁷ These interventions included IV-tPA administration in the CT scanner and a stroke code activation system. None of the improvement initiatives involved EMS. Mission Protocol also included paramedic education and real-time EMS provider feedback which likely has a multiplicative effect on future EMS stroke dispatches. Incorporating EMS into our streamlining processes likely accounts for this improvement in DTN times.

Though not statistically significant, the percentage of patients who received IV-tPA and were considered stroke mimics at final diagnoses was higher in the Mission Protocol group than the Year Prior group (16% versus 4.4%). The stroke mimics who received IV-tPA were seen primarily in the early implementation of Mission Protocol. A possible explanation for this phenomenon is unnecessarily expedited transfer to CT prior to full ED physician evaluation. None of these patients suffered sICH. The single sICH in our study was not a stroke mimic as there were ischemic changes and an occlusion in the distal right anterior cerebral artery territory on initial imaging.

There was no difference found in the median DTG artery puncture times for the limited number of thrombectomies performed during the study periods; however, the upper limit of the interquartile ranges was faster in the Mission Protocol group. It is possible that our sample was too small to detect improvements in thrombectomy metrics due to the Mission Protocol or that additional systems change, such as earlier activation of neurointerventional radiology or direct transport to a single imaging suite that can facilitate both thrombolysis and thrombectomy, may be required.

Limitations

Given this study was conducted at an urban, public safety net hospital with access to 24-hour neurology consultation, the findings of this study may be limited in generalizability. However, the diverse patient population treated, many who are socioeconomically disadvantaged and many speaking a language other than English as a primary language, highlights this protocol's applicability in varying populations. Another potential limitation of our study was the process of a Mission Protocol activation. Since it was the responsibility of the EMS triage nurse from ambulance prenotification, it is possible that some patients were not activated under this protocol due to nurse variation.

Conclusions

We found that implementation of the Mission Protocol, which emphasized an ED team-based approach from ambulance arrival to CT scanner, was associated with an increase in the rate of DTN times less than or equal to 45 minutes from 62% to 84%. Median door to CT and DTN times were also improved. Future studies may examine the impact of this type of protocol on nonstroke patients.

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Declaration of Competing Interest

Dr. Madhok, Ms. Cole, Ms. Martin, and Dr. Hemphill declare that they have no conflict of interest. Dr. Keenan reports grants from NIH StrokeNet Fellowship, outside the submitted work.

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