Modeling the Impact of Prehospital Triage on a True-Life Drip and Ship Mechanical Thrombectomy Urban Patient Cohort

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Abstract

Objective: The aim of the study was to model the effect of prehospital triage of emergent large vessel occlusion (ELVO) to endovascular capable center (ECC) on the timing of thrombectomy and intravenous (IV) thrombolysis using real-world data from a multihospital system. ***Methods:*** We selected a cohort of 77 consecutive stroke patients who were brought by emergency medical services (EMS) to a nonendovascular capable center and then transferred to an ECC for mechanical thrombectomy (MT) ("actual" drip and ship [DS] cohort). We created a hypothetical scenario (bypass model [BM]), modeling transfer of the patients directly to an ECC, based on patients' initial EMS pickup address and closest ECC. Using another cohort of 73 consecutive patients, who were brought directly to an ECC by EMS and underwent endovascular intervention, we calculated mean door-to-needle and door-to-arterial puncture (AP) times ("actual" mothership [MS] cohort). Timings in the actual MS cohort and the actual DS cohort were compared to timings from the BM cohort. ***Results:*** Median first medical contact (FMC) to IV thrombolysis time was 87.5 min (interquartile range [IQR] = 38) for the DS versus 78.5 min (IQR = 8.96) for the BM cohort, with p = 0.1672. Median FMC to AP was 244 min (IQR = 97) versus 147 min (IQR = 8.96) (p < 0.001), and median FMC to TICI 2B+ time was 299 min (IQR = 108.5) versus 197 min (IQR = 8.96) (p < 0.001) for the DS versus BM cohort, respectively. ***Conclusions:*** Modeled EMS prehospital triage of ELVO patients' results in shorter MT times without a change in thrombolysis times. As triage tools increase in sensitivity and specificity, EMS triage protocols stand to improve patient outcomes.

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Introduction

Since the advent of intravenous (IV) thrombolysis, patients with neurologic symptoms concerning for acute ischemic stroke have been brought by emergency medical services (EMS) to the nearest hospital designated as a stroke center. Patients undergo diagnostic imaging and, when appropriate, receive IV thrombolytics. Over the past decade, mechanical thrombectomy (MT) has become the standard of care for management of acute

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ischemic stroke caused by emergent large vessel occlusion (ELVO) [1]. For the purposes of this study, primary stroke centers are referred to as nonendovascular capable centers (nECCs), while thrombectomy capable centers and comprehensive stroke centers will be referred to as endovascular capable centers (ECCs). Once ELVO is diagnosed at a nECC, ELVO patients must be transferred to an ECC for MT. However, interhospital transfers have been associated with significant delays in treatment [2]. Earlier treatment times result in improved functional outcomes [3]. Prehospital triage protocols have been developed to improve prehospital recognition of ELVO and improve treatment times. During the period of this study, prehospital triage protocols were not being used by EMS personnel in New York City to identify ELVO patients who may be transported directly to ECCs.

The Mount Sinai Health System encompasses ECCs that receive patients from EMS and also receive transfers from multiple nECCs. The rate of stroke in the NYC EMS patient population is about 50 per 4,800 EMS calls (1%) [4]. The percentage of acute stroke patients who received IV thrombolysis and MT changed from 7.8% to 8.4% and from 1.3% to 2.6% since MT became standard of care [5]. We have previously published that treatment times are significantly delayed for patients requiring interhospital transfer [6–8]. We hypothesized that treatment times would be shorter if patients are initially triaged to ECCs and sought to explore this in a modeled cohort.

Methods

Data Collection

We performed a retrospective analysis of a prospectively collected institutional quality improvement database. Study protocols for data collection and this analysis were approved by our Institutional Review Board. Recorded data points included first medical contact (FMC) times, EMS departure times, EMS pickup addresses, nECC and ECC arrival times, IV thrombolysis administration times, arterial puncture times, recanalization times, and patient outcomes.

Patient Selection

Between September 1, 2017, and March 31, 2019, 287 consecutive patients underwent MT within our health system. Patients with both anterior and posterior circulation occlusions were included in this analysis. Patients were further stratified into those who attended a nECC prior to transfer for MT ("drip and ship" [DS] cohort) and those who were brought directly to an ECC by EMS ("mothership" [MS] cohort). In order to limit our analysis to the impact of prehospital EMS logistics on treatment times, inpatients who experienced inhospital ischemic stroke and underwent MT were excluded. Patients whose records had incomplete EMS data were excluded. Delayed decision-making regarding MT was also an exclusion factor. After these exclusions, 77 DS and 73 MS patients were analyzed. Baseline patient characteristics are shown in Table 1.

Modeling

We created a hypothetical "bypass model" (BM) cohort, by calculating the "modeled" times of the DS patients in the case that they would have been transferred directly to an ECC instead of a nECC, with EMS triage. Using FMC as time zero, a care timeline was created for each patient. Within the BM cohort, patients' EMS pickup addresses were geocoded and mapped using Google Maps Application Programming Interface. The closest ECC was identified based on driving distance and driving times, and ambulance driving times were calculated using traffic data from the actual date and time of pickup, using Google Maps Application Programming Interface. However, since BM is a hypothetical cohort, times for the intrahospital events were calculated using mean times for door to thrombolysis, door to AP, and door to thrombolysis in cerebral infarction (TICI) 2B+ recanalization from the MS cohort. Therefore, the differences between BM and MS cohorts are as follows: BM is modeled based on real DS patients, while MS is actual patient data; FMC to ECC is calculated based on geocoding for the BM cohort, while it consists of real-life data for the MS cohort; door to thrombolysis, door to AP, and door to TICI 2B+ recanalization for the BM cohort are the relative calculated means from the MS cohort (we selected the means for these time metrics from the MS and not the DS cohort, since both BM and MS patients are supposed to receive thrombolysis in the ECC, while DS patients stop by in a nECC to receive thrombolysis and then get shifted to an ECC). We looked at the outcomes of time from FMC to thrombolysis, FMC to AP, and FMC to recanalization.

Statistical Analysis

We used SAS software to perform our analysis. Transport times followed a normal distribution, and we reported their means and standard deviations, while treatment times were not normally distributed; therefore, we reported their medians and interquartile ranges (IQRs). Student's t test was conducted for comparing both the normally distributed and the non-normally distributed variables (since sample is >30 for the latter). We compared DS versus MS cohort and DS versus BM cohort. A p value of <0.05 was considered as the level of statistical significance for this study.

Results

Baseline characteristics of the cohorts are reported in Table 1. Mean central hospital NIH stroke scale was 17 versus 16 for DS and MS cohorts. Respectively, the number of patients who received IV thrombolysis was 34 versus 31 (44.2% vs. 42.5%), and pre-stroke modified Rankin score (mRS) was assessed as 0 in 42 versus 40 (54.5% vs. 54.8%) patients, 1 in 10 versus 10 patients, 2 in 9 versus 5 patients, and 3 or greater in 16 versus 18 patients. The M1 segment of the middle cerebral artery was the most common site of occlusion for both cohorts. All comparisons are shown in Tables 2 and 3, with the corresponding p

Matsoukas/Giovanni/Rubinstein/Majidi/
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Table 1. Baseline patient characteristics

Baseline cohort characteristics	DS (n = 77)	MS (n = 73)
Demographics and other information		
Age, median (SD)	73.4 (13.2)	72.8 (13.2)
Male sex, n (%)	33 (42.9)	32 (43.8)
Female sex, n (%)	44 (57.1)	41 (56.2)
Central hospital NIHSS, mean (SD)	17 (7)	16 (7)
Thrombolysis, n (%)	34 (44.2)	31 (42.5)
Medical history, n (%)		
Essential hypertension	66 (85.7)	46 (63)
Atrial fibrillation	37 (48.1)	29 (39.7)
Diabetes mellitus	34 (44.2)	22 (30.1)
Hyperlipidemia	22 (28.6)	26 (35.6)
Valvular heart disease	3 (3.9)	0 (0)
Chronic kidney disease	6 (7.8)	2 (2.7)
Ischemic stroke	12 (15.6)	14 (19.2)
Transient ischemic attack	5 (6.5)	2 (2.7)
Chronic heart failure	8 (10.4)	6 (8.2)
Coronary artery disease or myocardial infarction	13 (16.9)	11 (15.1)
Peripheral vascular disease	4 (5.2)	4 (5.5)
Pre-stroke mRS, n (%)		
0	42 (54.5)	40 (54.8)
1	10 (13)	10 (13.7)
2	9 (11.7)	5 (6.8)
≥3	16 (20.8)	18 (24.7)
Location of occlusion based on CTA, n (%)		
Internal carotid artery	0 (0)	1 (1.4)
Internal carotid artery terminus	16 (20.8)	12 (16.4)
Tandem occlusion	2 (2.6)	4 (5.5)
Middle cerebral artery M1	36 (46.8)	31 (42.5)
Middle cerebral artery M2	13 (16.9)	19 (26)
Middle cerebral artery M3	1 (1.3)	1 (1.4)
Anterior cerebral artery	0 (0)	1 (1.4)
Posterior circulation	9 (11.7)	4 (5.5)

DS, drip and ship; MS, mothership; mRS, modified Rankin score.

values. The mean EMS on-scene time for patients in the DS cohort was 21.3 min. Individual on-scene times were used for the BM cohort in each patient. Scene to first hospital (either nECC or ECC) transport times for DS versus MS were 8.6 min (SD = 5) and 9.6 min (SD = 5), respectively ($p = 0.13$). Mean scene to first hospital transport times were 8.6 min (SD = 5) for DS versus 10.7 min (SD = 3.7) for BM, $p = 0.0001$ (Table 2). Mean FMC to ECC time was 211.2 min (85.5) for DS and 32 min (8.96) for BM ($p < 0.001$). Mean total ambulance driving time, including the transfer, was 38.7 min (17.3) for DS and 10.7 min (3.68) for BM, $p < 0.001$ (Table 2).

Similarly, median door to IV thrombolysis time was 57 min (IQR = 39.25) in DS model versus 46.5 min (IQR N/A here) in the BM ($p = 0.011$), door to AP was 48 min (IQR = 24) versus 115 min (IQR N/A here), ($p < 0.001$), and door to TICI 2B+ was 92 min (IQR = 49) versus 165 min (IQR N/A here), ($p < 0.001$) for DS versus BM, respectively (Table 3). FMC to IV thrombolysis was 87.5 min (IQR = 38) versus 78.5 min (IQR = 8.96), $p = 0.1672$ (Table 3). Last, FMC to AP was 244 min (IQR = 97) versus 147 min (IQR = 8.96) ($p < 0.001$), and FMC to TICI 2B+ was 299 min (IQR = 108.5) versus 197 min (IQR = 8.96) for DS versus BM, respectively (Table 3). The aforementioned results are also graphically represented in Figure 1a, b.

Discussion

Using a real-life patient cohort from a stroke system of care within a large multihospital institution, we demonstrated that treatment times were shorter in a model of

Table 2. Transport times (means with standard deviations, in minutes)

DS versus MS	DS	MS	p value
EMS on-scene time	21.3 (8.4)	21.3 (8.9)	0.81
Scene to first hospital	8.6 (5)	9.6 (5)	0.13
FMC to nECC	29.9 (10.8)	N/A	–
Transfer	30.1 (15.9)	N/A	–
FMC to ECC	211.2 (85.5)	30.6 (10.2)	<0.001
Total ambulance	38.7 (17.3)	9.6 (5)	<0.001

DS versus bypass	DS	BM	p value
EMS on-scene time	21.3 (8.4)	N/A	–
Scene to first hospital	8.6 (5)	10.7 (3.7)	0.0001
FMC to nECC	29.9 (10.8)	N/A	–
Transfer	30.1 (15.9)	N/A	–
FMC to ECC	211.2 (85.5)	32.03 (8.96)	<0.001
Total ambulance	38.7 (17.3)	10.74 (3.68)	<0.001

EMS, emergency medical services; FMC, first medical contact; nECC, nonendovascular capable center; ECC, endovascular capable center; BM, bypass model; MS, mothership; DS, drip and ship.

**Table 3.** Treatment times (medians with IQRs, in minutes)

DS versus MS	DS	MS	p value
Door to IV thrombolysis	57 (39.25)	46.5 (22.5)	0.0465
Door to AP	48 (24)	115 (53)	<0.001
Door to TICI 2B+	92 (49)	165 (83)	<0.001
DIDO	126 (79)	N/A	–
FMC to IV thrombolysis	87.5 (38)	79 (18)	0.12
FMC to AP	244 (97)	151 (53.5)	<0.001
FMC to TICI 2B+	299 (108.5)	201 (83.5)	<0.001

DS versus bypass	DS	BM	p value
Door to IV thrombolysis	57 (39.25)	46.5 (N/A)	0.0110
Door to AP	48 (24)	115 (N/A)	<0.001
Door to TICI 2B+	92 (49)	165 (N/A)	<0.001
DIDO	126 (79)	N/A	–
FMC to IV thrombolysis	87.5 (38)	78.5 (8.96)	0.1672
FMC to AP	244 (97)	147 (8.96)	<0.001
FMC to TICI 2B+	299 (108.5)	197 (8.96)	<0.001

IV, intravenous; AP, arterial puncture; TICI, thrombolysis in cerebral infarction; DIDO, door in door out; FMC, first medical contact; BM, bypass model; MS, mothership; DS, drip and ship.

prehospital triage with direct routing to ECCs, while preserving time to IV thrombolysis in an urban environment. These data add to evidence that triaging patients in the field will improve time to thrombectomy for ELVO patients and may result in improved outcomes, especially in a high-density population area. New York City is a densely populated city with high availability of nECCs and ECCs. Another bypass modeling study reported median actual EMS arrival to arterial puncture time of 215 min versus modeled bypass scenarios time to a STRATIS registry ECC of 127 min ($p < 0.001$) and 121 min to the ideal ECC ($p < 0.001$) [9]. The difference in time reported in this study resulted in statistically significant differences in modeled 3-month disability [9]. When the patient is

Fig. 1. a Graphical representation of FMC to IV thrombolysis, FMC to AP, and FMC to TICI 2B+ times for all cohorts. **b** Graphical representation of metrics, for all cohorts, as follows: scene to nECC, DIDO, nECC to ECC, scene to ECC, and door to TICI 2B+ times. Door to TICI 2B+ times are the same between MS and bypass cohorts. We created the hypothetical BM assuming that only transport times would be different compared to the MS cohort. Door to TICI 2B+ time in the BM group includes IV thrombolysis and therefore is longer compared to the DS door to TICI 2B+ time. FMC, first medical contact; IV, intravenous; AP, arterial puncture; TICI, thrombolysis in cerebral infarction; nECC, non-endovascular capable center; DIDO, door in door out; ECC, endovascular capable center; DS, drip and ship; BM, bypass model; MS, mothership.
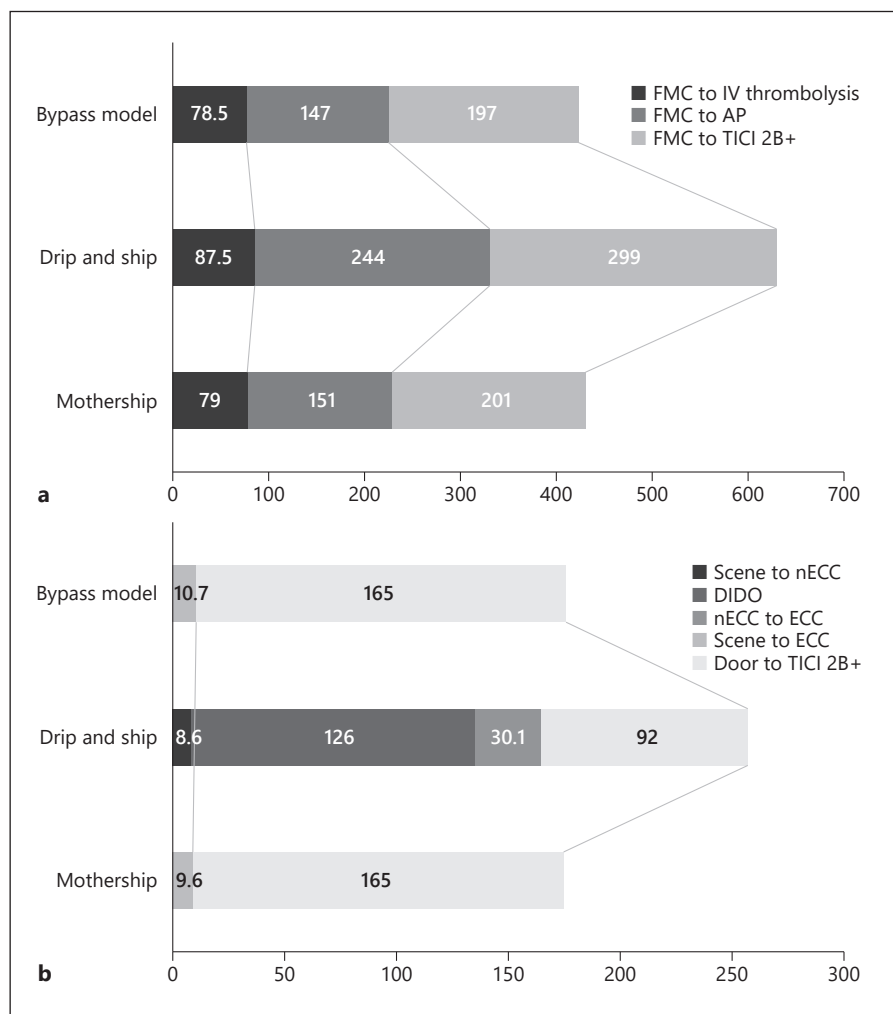
directly transferred to an ECC within 20 miles from the patient pickup point, MT can be achieved 94 min earlier, delaying thrombolysis by 7 minutes [9, 10], thus possibly ensuring eligibility for thrombolysis [9]. A recent meta-analysis including more than 2,000 patients from 9 studies reported better functional outcomes for patients treated via the MS versus the DS protocol (adjusted relative risk was 0.87, 95% CI 0.77–0.98, and unadjusted relative risk was 0.87, 95% CI 0.81–0.93, I^2 = 0.0%). However, reperfusion success and 90-day mortality did not differ statistically significantly [11]. Notably, eligibility for MT can be decreased up to 41% when rerouting patients from a nECC to an ECC due to either clinical improvement after thrombolysis or changes in neuroimaging [2]. In addition, interhospital transfer has been associated with longer onset-to-AP and onset-to-recanalization times [12, 13]. Our study confirms that routing ELVO patients di-

rectly to ECC centers should achieve shorter time final recanalization additionally, without the cost of delaying IV thrombolysis, in the urban setting.

Different mathematical models have been developed aiming to model treatment times of ELVOs based on geocoding and patient characteristics [14–17]. The pre-hospital transport decision-making is context-specific, and geographical distance from scene, transport times (based on map applications), treatment times at both nECC and ECC, as well as accuracy of available triaging tools have been advocated to be the most important determinants for such a decision [14, 17]. Milne et al. developed probability models based on the ESCAPE trial's decay curves in order to calculate and compare the probability of good outcomes (PGO) (90-day mRS score 0–2) between the DS and MS protocols. The authors concluded that when a nECC can achieve door-to-needle times

less than 30 min, DS is favored [15]. In continuation of this work, Holodinsky et al. [17] supported that DS and MS achieved similar modeled PGOs when the driving distance between the nECC and ECC was 60 min or less, by applying probability modeling. Similarly, Ali et al. [16] developed a mathematical model that provides location-based optimal EMS routing choices using real-time data. Importantly, this model differs from previously done work, as it incorporates the possibility of different diagnoses, the diagnostic uncertainty of the triaging scales used at the field as well as the up-to-date performance of the different target hospitals. In contrast to the previously mentioned PGO studies, its output refers to cost and quality-adjusted life-years, thus providing a clinical instead of a probabilistic answer.

Utilization of screening scales for ELVO can result in more efficient patient workflow and achieve lower treatment times in both thrombolysis and endovascular treatments [18]. Already existing scales include the Los Angeles Motor Scale (LAMS), the Rapid Arterial Occlusion Evaluation (RACE), the Vision, Aphasia, Neglect, the Field Assessment Stroke Triage for Emergency Destination, the 3-step ambulance clinical triage for acute stroke treatment algorithm [19], and the Cincinnati Prehospital Stroke Severity Scale. It is important to note that a review of currently existing triage scales for ELVO supported that different scales may have a different sensitivity and/or specificity in different settings (field, emergency department) [20]. The Stockholm Stroke Triage System (SSTS), which includes a physical exam for hemiparesis, real-time screen by a nurse, and a tele-health assessment by a stroke expert, achieved 95% specificity in both detecting ELVO and the need for MT [21]. In addition, specificity and overall accuracy were statistically significantly higher in the patient group that presented within 6 h after symptoms onset [21]. In a case-control study, triaging stroke patients with SSTS in the field resulted in faster MT times without delaying IV thrombolysis [22]. The RACE scale performed by EMS personnel has greater sensitivity compared to the SSTS scale, strong positive correlation with NIHSS score ($r = 0.76$) but poor specificity and positive predictive value [23]. Remarkably, specificity and positive predictive value were lower when RACE was implemented in stroke triage by US EMS personnel in a retrospective study [24]. The Cincinnati Prehospital Stroke Severity Scale did not differ statistically significantly from other currently used triaging systems in ELVO predictive performance [25]. In a prospective study, the use of LAMS proved superior compared to

the conventional protocol of transferring patients to the nearest stroke hospital using geocoding [26]. Ultimately, this could lead in a substantially decreased number of secondary transfers [26]. False-negative results might include cases with good collateral circulation, in whom delays can be tolerated with less resultant morbidity [19]. On the other hand, hemorrhagic strokes that are falsely identified as ELVOs will still benefit if shifted to an ECC, where neurosurgical support is readily available [19]. Nevertheless, the exact impact of ELVO triaging scales has to be determined in large prospective trials. A new clinical triage scale for bypass, called S-LAMS, is now being utilized by NYC EMS personnel in order to shift potential ELVOs to ECCs. The accuracy of this scale is not yet known.

Identifying MT-eligible patients in the field is a new challenge stemming from the ability to perform MT, while axial imaging serves as the gold standard method for identifying an ELVO. Technological improvements may further improve results. It has been reported that mobile stroke units could serve the role of primary stroke centers, administering IV thrombolysis and performing CT angiogram [27]. This, in conjunction with artificial intelligence, could expedite treatment and result in better functional outcomes. However, not every mobile stroke unit is capable of performing CT angiography, and it is not widely available in many cities. Therefore, clinical triage may be the only means for identifying ELVO patients at this current time. Importantly, these scales have a small learning curve and require minimal training. Triage tools for patients with ELVO in a densely populated area can potentially result in no delay in IV thrombolytic administration, with decreased onset-to-AP time and better 90-day outcomes [28]. The establishment and utilization of protocols that include early ECC notification and electronic platforms for instant image sharing can enhance treatment times and ensure better outcomes [29]. As far as limitations are concerned, our study tested a hypothetical model in a large city where there is proximity between nECCs and ECCs. Results may not be applicable to rural areas or in cities where these centers are sparsely dispersed on the map. In addition, our results may be markedly affected not only by geography, distances, travel times (this city has some of the highest densities of stroke units), weather, and traffic conditions, but also by the inhospital workflow of the individual hospital. Further work could evaluate the impact of triage scales on early and long-term clinical outcomes post-MT as these tools are being implemented in the real-life scenario.

Conclusion

Based on our model, triaging patients with possible ELVO to the closest ECC is effective, resulting in earlier treatment times for ELVO patients compared to a DS cohort. Importantly, direct triage does not appear to sacrifice any valuable time in IV thrombolytics administration in the urban setting. This practice could potentially enhance long-term outcomes by affording faster treatment times with the proper implementation of triage tools by EMS.

Statement of Ethics

IRB approval was obtained by the Human Research Protection Program at the Icahn School of Medicine at Mount Sinai (ISMMS), and informed consent was waived due to the retrospective nature of the study (19-1975-00001-01).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.F. conceptualized the project. S. Matsoukas collected, analyzed, and interpreted the data, and drafted and significantly edited the manuscript and figures. All authors made final edits to the manuscript.

Data Availability Statement

Fully anonymized data are available and can be provided by the corresponding author, upon reasonable request.

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