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Original Article

Impact of code stroke on thrombolytic therapy in patients with acute ischemic stroke at a secondary referral hospital in Taiwan

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Abstract

Background: Efficacy of thrombolytic therapy decreases with time elapsed from symptom onset. We sought to identify the impact of code stroke on the thrombolytic therapy.
Methods: Code stroke is activated by the emergency physician when a patient is eligible for thrombolytic therapy. We retrospectively reviewed patients with acute ischemic stroke between January 2011 and December 2014.
Results: In total, 1809 patients were enrolled. Code stroke was activated in 233 of 351 patients arriving at the emergency room (ER) within 3 h of symptom onset, and in 21 patients arriving >3 h. The sensitivity, specificity, and positive and negative predictive values of code stroke were 76%, 46%, 72%, and 51%, respectively. Thrombolytic therapy was provided to 58 patients, accounting for 3.4% of all cerebral infarcts. Code stroke was activated in 40 of these patients. The most common reasons for excluding thrombolytic therapy were: National Institute of Health Stroke Scale (NIHSS) < 6, intracranial hemorrhage (ICH), and age >80 years. Mean liaison-to-neurological evaluation time was only 6 min. Code stroke activation significantly reduced all the intervals, except for the onset-to-ER and door-to-order times. During the 4-year study period, there were significant reductions of the door-to-neurology liaison time by 28 min and door-to-laboratory time by 22 min. The proportion of door-to-needle time within 60 min improved from 33% in 2011 to 67% in 2014. Improved NIHSS scores during hospitalization were most prominent in tPA-treated patients. Symptomatic ICH occurred in 3.6% patients arriving within 3 h. Death occurred in 50% of patients received tPA treatment on family's request, and only 13% of those patients had favorable outcome.
Conclusion: Code stroke is effective in reducing in-hospital delays. The accuracy of code stroke activation has acceptable sensitivity but low specificity. Rapid patient assessment by neurologists increases the number of patients eligible for thrombolytic therapy.

Keywords: Acute stroke; Brain infarction; Code stroke; In-hospital delays; Thrombolytic therapy

1. Introduction

Intravenous thrombolytic therapy with tissue plasminogen activator (tPA) is the only pharmacological treatment that has been proven effective for acute ischemic stroke within 3–4.5 h from symptom onset.[1] The efficacy of thrombolytic therapy decreases with time elapsed from symptom onset. In-hospital delay is the time interval from hospital presentation to the loading bolus of tPA. The National Institute of Neurological Disorders and Stroke (NINDS) guidelines provided recommendations for specific in-hospital time intervals of 60 min from the door to drug administration.[2] Invisible in-hospital delays are usually present even in comprehensive stroke centers despite of efforts for time reduction.

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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Stroke performance measures (or quality metrics) are crucial for the improvement of stroke treatment quality and patient outcomes.[3,4] A well-organized standardized pathway (code stroke) does not per se guarantee a timely thrombolytic therapy. The Taiwan Stroke Registry revealed that several performance measures must be improved to achieve the requisite standard of care to fulfill the Get With The Guidelines-Stroke program in the United States.[5,6] The Institute for Healthcare Improvement, which seeks to improve health care by supporting process change, conducted the Breakthrough Series (BTS)−Stroke activity from August 2010 to July 2011 in Taiwan. More than 24 hospitals participated in this activity and attempted to improve the quality of stroke care through model learning and experience sharing.[4] The present study investigated the impact of code stroke activation on the efficacy of thrombolytic therapy for acute ischemic stroke.

2. Methods

In the neurological department, the responsibility of code stroke is assigned to eight consultant neurologists according to a regular schedule. After serial interventions to reduce treatment delays from participation in the BTS-stroke activity in 2010, a newly established code stroke protocol for intravenous thrombolytic therapy has been implemented in this hospital. Code stroke is activated by the emergency physician when a patient is eligible for evaluation of thrombolytic therapy, i.e, aged between 18 and 80 years old arriving at the ER within 2 h of symptom onset with positive Cincinnati Prehospital Stroke Scale.[7] The standard procedure includes a rapid transportation of the patient from the triage area to the first-aid area, followed by a computerized order entry for an immediate brain CT scan, a blood test, as well as an emergency consultation to the on-duty neurologist, both in-person contact and message through a mobile phone (stroke call). Pneumatic tube systems for a rapid delivery of blood samples and a direct hot line telephone from the ER to the laboratory department were established to confirm first-priority blood tests. Video-assisted therapeutic risk information, which illustrates the pathophysiology of acute ischemic stroke, tPA mechanism, and the overall risks and benefits of the treatment, was provided to the patient or family members through a 3-min animated video before obtaining informed consent.[8] We followed the treatment guideline of the Taiwan Stroke Society[9] and the reimbursement criteria of the Bureau of National Health Insurance.[10] The major criteria for tPA treatment were within 3 h of symptom onset, age between 18 and 80 years, and National Institute of Health Stroke Scale (NIHSS) score between 6 and 25. Patients received an intravenous dosage of tPA (0.6−0.9 mg/kg) under the recommendation of the Taiwan Stroke Society according to the results of NINDS[11] and Japan Alteplase Clinical Trial.[12]

For continuous quality control, we prospective registered patients who were sent to the ER for stroke or transient ischemic attack (TIA), and for suspected stroke with activation of code stroke. We retrospectively reviewed all the registered patients during the period from January 2011 to December 2014. The main outcomes of interest were the accuracy of code stroke activation, door-to-needle time (the time from patient presentation to the intravenous loading bolus of tPA), and functional outcome of patients after thrombolytic therapy. In addition, other structural time intervals, including onset-to-ER, door-to-order, door-to-CT, door-to-neurology liaison, liaison-to-neurology evaluation, door-to-laboratory, door-to-consent, consent-to-needle, and door-to-needle times, were also analyzed. Patients with an increase of two or more points in their NIHSS scores during the acute stroke stage were defined as experiencing clinical deterioration.[13,14] Outcomes were evaluated using the NIHSS, Barthel index and modified Rankin Scale (mRS) at discharge. An mRS score of $\leqq 2$ was considered an indicator of favorable outcome.

A two-sample t test and analysis of variance were conducted to evaluate the differences in the means of continuous variables. A p value of <0.05 was considered statistically significant. All statistical analyses were computed using SPSS (version 24, SPSS, Inc. Chicago, IL, USA). This study was approved by the Institutional Review Board of the Hospital (06-XD04-009).

3. Results

In total, 1809 patients were enrolled in the study. Among them, 1705 patients were final diagnosed as cerebral infarct. Fig. 1 presents the patient enrollment flowchart. There were 351 patients (19.4%) with suspected acute stroke presented at the ER within 3 h of symptom onset, and 100 patients (5.5%) presented at the ER at 3−4 h from symptom onset. Code stroke was activated in 233 of 351 patients arriving within 3 h, and in 21 of 1458 patients arriving >3 h of symptoms onset. Code strokes were initiated outside of office hours in 61% of patients. Table 1 presents the final diagnosis and distribution of code stroke in 372 patients with suspected acute stroke. Intracranial hemorrhage (ICH) and stroke mimics accounted for 16% and 14% of code strokes, respectively. There were 241 patients eligible for evaluation of thrombolytic therapy, and code stroke was not activated in 58 patients (24%). The percentage of missing activation of code stroke dropped yearly from 30% in 2011 to 11% in 2014. Given that a neurological liaison was initiated before an available brain CT result during the code stroke to save more time, patient who fulfilled the aforementioned criteria but were later found to have ICH were still considered to have accurate code stroke activation. The sensitivity, specificity, and positive and negative predictive value of code stroke activation were 76%, 46%, 72%, and 51%, respectively. The positive and negative likelihood ratios for code stroke were 1.41 and 0.74, respectively.

A total of 58 patients received tPA treatment, comprising 3.4% of all cerebral infarcts, and code stoke was activated in 40 of the 58 patients. Eight patients (one with and seven without code stroke activation) did not fulfill the criteria for thrombolytic therapy still received tPA treatment because of a strong request from their family members. In total, 51 patients fulfilled the criteria, of which 50 patients (98%) received tPA

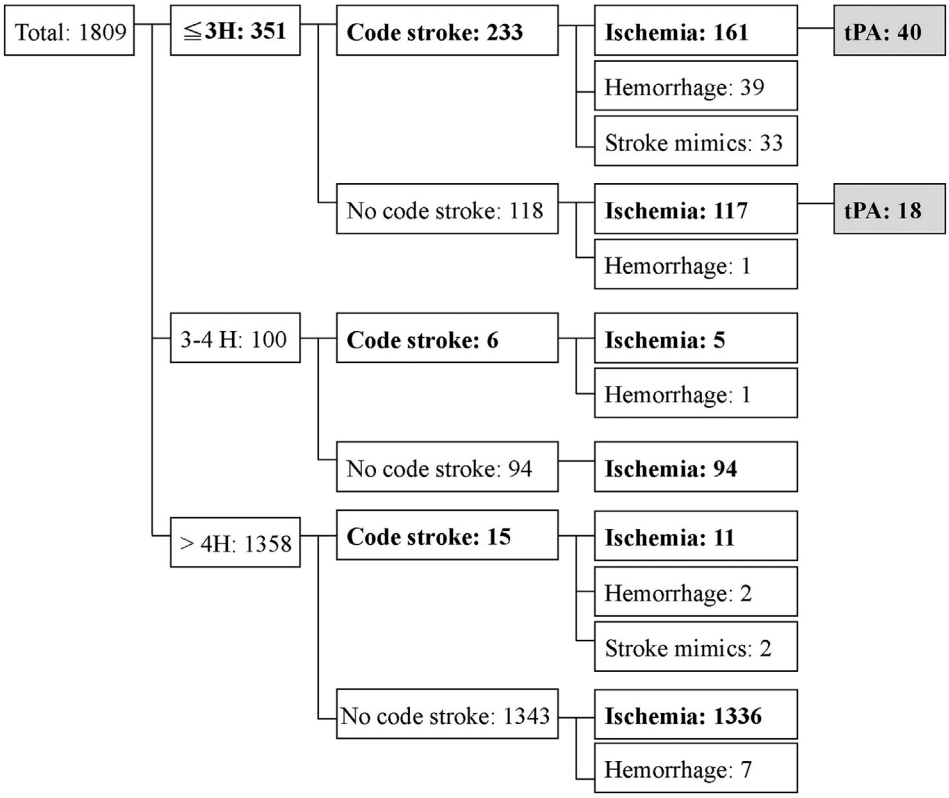

Fig. 1. Flowchart of patient enrollment. tPA, tissue plasminogen activator.

Table 1
Final diagnosis and code stroke in 372 patients with suspected acute stroke.

	Code stroke[b] (n = 254)	No code stroke (n = 118)
Final diagnosis		
Infarct (n = 264)	155	109
Transient ischemic attack (n = 30)	22	8
Intracranial hemorrhage (n = 43)	42	1
Stroke mimics (n = 35)	35	0
Thrombolytic therapy		
Eligible[a] (n = 241)	183	58
Non-eligible (n = 131)	71	60

[a] Eligible: onset ≦ 3 h, age 18–80 years, positive Cincinnati Prehospital Stroke Scale.
[b] Includes 233 patients who presented within 3 h of symptom onset and 21 patients who presented at >3 h from symptom onset.

Table 2
Reasons for excluding thrombolytic therapy in 293 patients who presented within 3 h of symptom onset.

Reasons	No.	%	Reasons	No.	%
NIHSS <6	119	30.9	Hyperglycemia or hypoglycemia	5	1.3
Intracranial hemorrhage	50	13.0	Uncontrolled blood pressure	5	1.3
Age >80 years	48	12.5	End stage renal disease	5	1.3
Stroke mimics	28	7.3	Refused to consent	5	1.3
Transient ischemic attack	27	7.0	Ischemic stroke within 3 months	4	1.1
NIHSS >25	18	4.7	International normalized ratio >1.3	4	1.1
Seizure	14	3.6	History of spine surgery	2	0.5
Unclear onset time	12	3.1	Severe head trauma	2	0.5
Diabetes + old stroke	10	2.6	Major surgery within 14 days	1	0.3
Gastrointestinal bleeding	8	2.1	Concurrent myocardial infarct	1	0.3
Old intracranial hemorrhage	7	1.8	Pregnancy	1	0.3
Onset time >2.5 h	7	1.8	No alteplase available	1	0.3
Total				384[a]	100.0

NIHSS = National Institute of Heath Stroke Scale.
[a] One or more important reasons may be present for a patient, such as age >80 years and NIHSS <6.

treatment. Only one patient who fulfilled the criteria but did not receive tPA treatment because of alteplase unavailability in the pharmacy department. Table 2 lists the main reasons for excluding intravenous tPA treatment in other 293 patients who presented at the ER within 3 h of symptom onset. The most common reasons for excluding thrombolytic therapy were: NIHSS <6 (31%), ICH (13%), age > 80 years (13%), stroke mimics (7%), and TIA (7%).

Table 3 shows the average intervals of in-hospital delays in 351 patients who presented at the ER within 3 h of symptoms onset. The overall mean onset-to-ER time was 70 min. The mean door-to-order, door-to-CT, and door-to-laboratory times were 6, 18, and 50 min, respectively. The mean liaison-to-neurological evaluation time was only 6 min. Patients with TIA had longer door-to-order time and door-to-neurology liaison time than those with ICH ($p < 0.05$). During the 4-

Table 3
In-hospital delay in 351 patients who presented within 3 h of symptom onset.

Characteristics	Onset-to- ER time	Door-to-Order time	Door-to-CT time	Door-to-neurology liaison time	Liaison-to-neurological evaluation time	Door-to-laboratory time	Door-to- consent time (n = 58)[a]	Consent-to-needle time (n = 58)[a]	Door-to- needle time (n = 58)[a]	Onset-to-needle time (n = 58)[a]
Total (n = 351)	70 ± 44	6 ± 4	18 ± 36	39 ± 91	6 ± 5	50 ± 90				
Infarct (n = 240)	71 ± 43	6 ± 3	18 ± 42	42 ± 93	6 ± 6	54 ± 106				
TIA (n = 38)	76 ± 50	8 ± 5*	28 ± 32	79 ± 140*	8 ± 7	54 ± 51				
ICH (n = 40)	60 ± 39	5 ± 5	12 ± 10	9 ± 8	4 ± 3	36 ± 18				
Stroke mimics (n = 33)	71 ± 42	6 ± 2	13 ± 6	14 ± 10	5 ± 4	39 ± 10				
Trends by year (n = 351)										
2011 (n = 88)	70 ± 42	6 ± 4	18 ± 25	54 ± 90	6 ± 7	61 ± 69	79 ± 49	10 ± 5	90 ± 53	132 ± 64
2012 (n = 76)	77 ± 43	6 ± 3	17 ± 13	42 ± 101	7 ± 6	46 ± 18	58 ± 23	15 ± 10	73 ± 23	131 ± 34
2013 (n = 102)	68 ± 47	7 ± 4	15 ± 14	36 ± 90	7 ± 5	53 ± 144	58 ± 29	16 ± 15	75 ± 28	130 ± 43
2014 (n = 85)	68 ± 43	6 ± 3	14 ± 10	26 ± 83*	5 ± 4	39 ± 57*	55 ± 26*	6 ± 4	61 ± 27	124 ± 49
Activation of code stroke										
Code stroke (n = 233)	68 ± 43	6 ± 3	13 ± 9**	12 ± 11**	5 ± 4**	37 ± 14**				
No code stroke (n = 118)	73 ± 45	7 ± 4	27 ± 59	90 ± 139	8 ± 7	76 ± 147				
Intravenous tPA (n = 58)	56 ± 38	6 ± 3	14 ± 15	17 ± 19	5 ± 4	40 ± 19	61 ± 33	12 ± 10	73 ± 34	129 ± 47
Code stroke (n = 40)	62 ± 40	6 ± 3	11 ± 7*	12 ± 9**	5 ± 3	36 ± 15*	54 ± 22*	9 ± 7*	63 ± 23**	125 ± 45
No code stroke (n = 18)	43 ± 28	6 ± 2	22 ± 23	29 ± 27	6 ± 5	51 ± 22	79 ± 46	16 ± 14	95 ± 45	138 ± 51

CT = computed tomography; ER = emergency room; ICH = intracranial hermorrhage; TIA = transient ischemic attack; tPA = tissue plasminogen activator.
*ANOVA test $p < 0.05$, **Two sample t test $p < 0.001$.
[a] Patients received intravenous thrombolytic therapy.

year study period, the door-to-neurology liaison and door-to-laboratory times were significantly reduced from 54 to 26 min ($r^2 = 0.172$, $p = 0.001$) and from 61 to 39 min ($r^2 = 0.191$, $p < 0.001$), respectively. All intervals, except for onset-to-ER and door-to-order times, were significantly reduced in patients with code stroke activation ($p < 0.001$). In 58 patients who received intravenous tPA treatment, code stroke activation significantly reduced the door-to-CT, door-to-neurology liaison, door-to-laboratory, door-to-consent, consent-to-needle, and door-to-needle times. The proportion of door-to-needle time within 60 min improved from 33% in 2011 to 67% in 2014 (Fig. 2). Moreover, a yearly secular trend of the door-to-needle time reduced from 90 min in 2011 to 61 min in 2014 was observed ($r^2 = 0.851$, $p = 0.078$). However, it did not reach a statistical significance owing to too short duration for analysis.

Only 51 of 193 patients (26%) with cerebral infarcts fulfilled the criteria for thrombolytic therapy, and 50 of these 51 patients received tPA treatment based on their doctor's decision. Table 4 presents a comparison of the clinical features and outcomes among 193 patients with cerebral infarcts eligible for intravenous thrombolytic therapy. The median initial NIHSS score was higher in patients who received tPA treatment based on their doctor's decision (13; mean = 13 ± 6) than

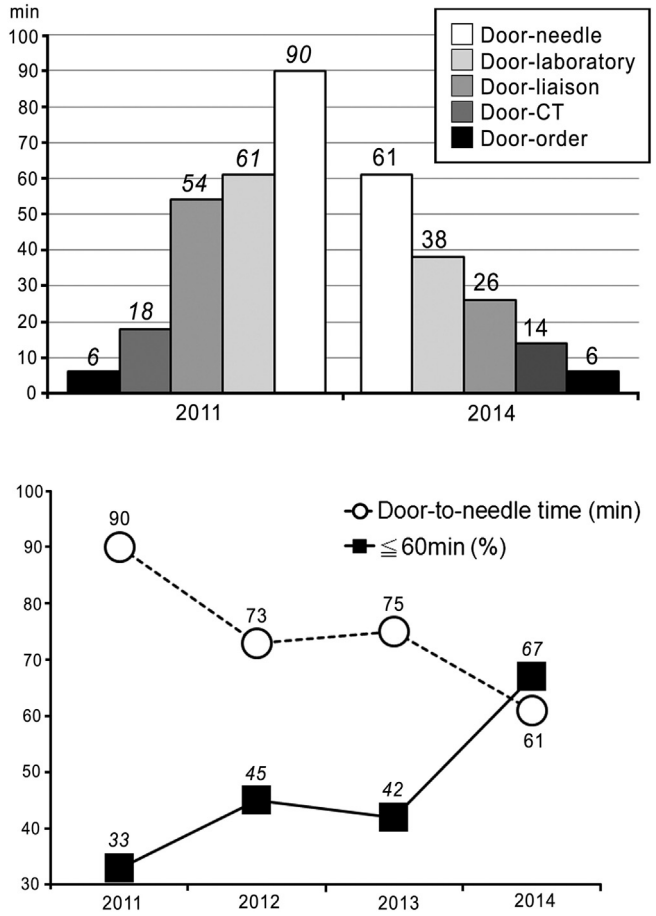

Fig. 2. Decreased in-hospital delays compared with 2014 to 2011 (upper). Decreased door-to-needle time and increased proportion of door-to-needle time within 60 min from 2011 to 2014 (lower).

Table 4
Clinical characteristics of 193 patients with cerebral infarct eligible[a] for evaluation of intravenous thrombolytic therapy.

Characteristics	No tPA treatment (n = 135)	tPA treatment by doctor (n = 50)	tPA treatment by request (n = 8)	*p*
Age (years)[b]	66 (58–74)	70 (61–75)	70 (63–78)	0.154
Male Sex[c]	85 (63%)	35 (70%)	5 (63%)	0.667
Initial NIHSS[b]	3 (2–11)	13 (8–18)	27 (6–32)	<0.001
Deterioration[c]	15 (11%)	12 (24%)	6 (75%)	<0.001
Symptomatic ICH[c]	3 (2.2%)	3 (6.0%)	1 (12.5%)	0.186
Discharge NIHSS[b]	2 (1–8)	6 (2–11)	36 (12–42)	<0.001
Discharge BI[b]	90 (50–100)	55 (21–99)	0 (0–41)	<0.001
Improvement of NIHSS	1 (0–3)	5 (1–9)	−6 (−10–−1)	<0.001
Discharge mRS[b]	1 (1–4)	4 (1–4)	6 (4–6)	0.002
Discharge mRS ≦ 2[c]	77 (57%)	20 (40%)	1 (13%)	0.009
Death[c]	3 (2%)	3 (6%)	4 (50%)	<0.001

Data are expressed as median (IQR) or n (%).
BI = Barthel index; ICH = intracranial hemorrhage; mRS = modified Rankin scale; NIHSS = National Institute of Heath Stroke Scale; tPA = tissue plasminogen activator.
[a] Eligible: onset ≦ 3 h, age ≦ 80 years, cerebral infarct (four patients who received tPA treatment were >80 years old).
[b] Kruskal–Wallis test.
[c] Chi-square test.

in those without tPA treatment (3; mean = 7 ± 8), and was highest in patients who received tPA treatment on their family's request (27; mean = 21 ± 15; $p < 0.001$). Median improvement of NIHSS scores during hospitalization were most prominent in patients who received tPA treatment based on their doctor's decision (from 13 to 6) compared with those in patients without tPA treatment (from 3 to 2) and those who received tPA treatment on their family's request (dropped from 27 to 36; $p < 0.001$). Clinical deterioration occurred in 31 of 193 patients (17%) and was most prominent in patients who received tPA treatment on their family's request (75%; $p < 0.001$). Symptomatic ICH occurred in 7 of 193 patients (3.6%), of which, three (6%) received tPA treatment based on their doctor's decision and one received tPA treatment on their family's request (12.5%). However, no significant difference was observed due to small sample size. Patients who received tPA treatment on their family's request had the lowest median Barthel index (0; mean = 26 ± 40) and highest mRS (6; mean = 5 ± 2) scores at discharge. Death occurred in 50% of patients who received tPA treatment on their family's request, and only 13% of them had favorable outcome with an mRS score ≦2.

4. Discussion

Emergency physicians have been exhibited to have high sensitivity and a positive predictive value of approximately 90% in identifying patients with stroke or TIA.[15] However, it is more difficult to screen patients who are eligible for thrombolytic therapy within very short period, such as 10–20 min. The sensitivity (76%) and positive predictive value (72%) of code stroke activation at the ER in the present study are comparatively acceptable and are close to the value of 72% reported on the Cincinnati Prehospital Stroke Scale for the presence of any three signs (arm weakness, speech, and facial droop).[16] The specificity was considerably low. Of the 51 patients received intravenous tPA treatment, 11 (22%) fulfilled the criteria but without code stroke activation. The rapid arrival of neurologists to the ER (only 6 min) after a neurological liaison helps improve the execution rate of thrombolytic therapy by not only reducing in-hospital delays but also identifying more patients eligible for treatment. For emergency consultations other than stroke calls from the ER, neurologists still arrived at the ER within 30 min. Meanwhile, 61% of the patients with code stroke activation were initiated outside the office hours. Moreover, 40 of the 254 patients with code strokes activation received intravenous tPA treatment, implying that only one patient was suitable for thrombolytic therapy per six stroke calls to the neurologists. Sung et at reported a mismatch between number of activation and number of thrombolysis.[17] In there study, only 12% of all the code stroke patients received thrombolytic therapy.

Similar to other studies, the major reason for excluding thrombolytic therapy in our study was NIHSS <6, including minor stroke and rapid clinical improvement.[18] With the improved treatment results and substantial clinical evidence, the exclusion criteria for intravenous tPA treatment are not so restrictive as earlier.[19] The Taiwan Stroke Society suggested the removal of the criterion age >80 years from absolute contraindication and the reduction of the lower limit of NIHSS score from 6 to 4 recently.[9] A new guideline from the Taiwan Stroke Society is being established to save more patients and help physicians in clinical practice. If the new guideline was applied in this study, an additional 42 patients would fulfill the criteria for tPA treatment, including 24 patients with a NIHSS score of 4–5 and 18 patients aged >80 years. Therefore, along with the 58 patients who received tPA treatment, the total thrombolytic rate might increase from 3.4% to around 6%. Nevertheless, a previous report found that increasing eligibility for tPA does not increase the rate of treatment, possibly due to the high symptomatic intracerebral hemorrhage rate among Chinese-Taiwanese.[20]

Code stroke activation significantly reduced the time intervals of door-to-CT, door-to-neurology liaison, liaison-to-

neurological evaluation, and door-to-laboratory. Because of the turn-over rate of physicians and nurses who resign from ER work, repeated education of the code stroke protocol and regular assessment of performance quality are necessary. This is the reason for the significant trends of annual improvement in the door-to-neurology liaison and door-to-laboratory times from 2011 to 2014. Similar annual improvement in the door-to-consent, consent-to-needle, and door-to-needle times were observed in patients received thrombolytic therapy. The door-to-laboratory time is the most time-consuming interval, particular for a final result of prothrombin time. The average door-to-neurological evaluation time was 22 min in tPA-treated patients. An experienced neurologist may require 15−20 min to interpret a brain CT scan and to complete a checklist (including NIHSS evaluation) for possible thrombolytic therapy. An average door-to-laboratory time of 40 min in this study just met the requirement of the final decision by neurologists. Informed consent is still necessary before intravenous tPA in Taiwan. A 21-min gap was present between door-to-laboratory and door-to-consent times. This gap was influenced by various factors, including delayed judgment by neurologists, the hesitation of patients or family members in receiving treatment, or the absence of relatives with the decision-making responsibility. The average consent-to-needle time was 12 min. Although this average time was reduced to 6 min in 2014, an immediate bolus of tPA within 3 min after obtaining informed consent is possible through a more convenient drug delivery protocol. Smith et al. and Acheampong et al. have demonstrated that bolus to infusion delays or interruptions in tPA infusion after the loading bolus may significantly affect serum tPA levels and reduce the efficacy of thrombolysis.[21,22]

With the help of an improved performance quality, we successful reduced the average door-to-needle time from 90 min in 2011 to 61 min in 2014 in all patients, and to 56 min in patients with code stroke activation (not shown in Table 3). The proportion of patients who received thrombolytic therapy within 60 min increased from 33% in 2011 to 67% in 2014. These achievements are ongoing and continue improving. Although only 26% of eligible patients fulfilled the criteria for thrombolytic therapy, 98% of these patients received tPA treatment. Improved NIHSS scores were most prominent in patients who received tPA treatment based on doctor's decision. Both minor and severe degrees of stroke severity were observed in patients without tPA treatment. Patients with minor stroke usually improved rapidly, while those with severe stroke might have aggravated outcomes. This could explain why patients without tPA treatment showed only a 2-point improvement in their NIHSS scores at discharge. Symptomatic ICH occurred in 6% of the patients who received tPA treatment based on their doctor's decision, which is similar to the occurrence rate (6.4%) reported by the NINDS in 1995.[11] Despite having higher initial NIHSS score, 40% of the patients who received tPA treatment based on doctor's decision had favorable outcomes. The low percentage of favorable outcomes and high mortality rate observed in the patients who received tPA treatment on family's request indicate that the violation of treatment protocol does not improve the quality of stroke care. The average dose of tPA in 58 patients was 0.75 mg/kg, which was lower than that recommended by the NINDS. Chao et al. reported that the standard tPA dose of 0.9 mg/kg may not be optimal for treating older Chinese patients.[23] In elderly patients (71−80 years), a lower tPA dose of 0.6 mg/kg yields improved outcomes.[24] The newly developed endovascular thrombectomy within 6−8 h of symptoms onset, with or without preceding intravenous tPA treatment, has been proved to improve functional outcomes and reduce mortality.[25−28] Intravenous thrombolytic therapy and dose of tPA may not play a crucial role in candidate patients for endovascular thrombectomy compared with those for intravenous thrombolytic therapy alone.

The present study did not observe any improvement in the onset-to-ER time from 2011 through 2014. Previous reports also found that an organized stroke team with standardized stroke pathways could reduce in-hospital delays. Educational efforts should include the training of ER physicians and other medical personnel.[29] In the present study, additional efforts can be taken to reduce in-hospital delays, including advanced courses for improving acute stroke identification on patient's arrival at the ER, the immediate loading bolus of tPA after obtaining the informed consent, and possibly, a rapid loading bolus ahead of the laboratory result of prothrombin time.[19,30] There are more infrastructural measures can be adopted for reducing in-hospital delays in endovascular thrombectomy, which enrolls neuroradiological group, with a longer time window up to 8 h.

The present study has some limitations. Firstly, this single hospital-based study had relatively small sample size. We could not stratify patients with tPA treatment for further analysis. However, the present study reflects the real-world efficacy of intravenous thrombolytic therapy at a secondary referral center in a community. The patient-centered but neurologist-directed 24-h emergency thrombolytic and thrombectomy therapies are highly demanding tasks. The workload and burn-out phenomenon of neurologists has led to a neurophobia to young doctors and hence become a new challenge for treatment quality maintenance in Taiwan.[31,32] Secondly, because of inadequate data, we could not compare the differences between the period of present study with newly established code stroke and the earlier period before 2011 with loose protocol. Only 12 patients received intravenous tPA between 2005 and 2010. Nevertheless, with the standard code stroke and a successful learning curve, we treated nearly five times as many patients in the following four years.

In conclusion, code stroke is effective in reducing in-hospital delays and the door-to-needle time in thrombolytic therapy for acute ischemic stroke. Code stroke activation has acceptable sensitivity but low specificity. A rapid expert assessment of patients by neurologists apparently increases the number of patients eligible for thrombolytic therapy. Additional efforts are being made to reduce in-hospital delays in endovascular thrombectomy.

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