

Original Article

Nationwide "Hospital Emergent Capability Accreditation by Level–Stroke" Improves Stroke Treatment in Taiwan

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Background and Purpose Recombinant tissue plasminogen activator (rtPA) is one of the proven therapies that improve the outcome of patients with acute ischemic stroke (AIS). In 2009, the Ministry of Health and Welfare, Executive Yuan, Republic of China, launched the project "Hospital Emergent Capability Accreditation by Level-Stroke (HECAL-Stroke)" to improve AIS treatment in Taiwan. The current study was performed to determine whether the project launched by the government was effective in promoting rtPA therapy among AIS patients.

Methods All participating hospitals were verified and designated as "heavy duty (HD)," "moderate duty (MoD)," or "medium duty (MeD)" according to the stroke center criteria. Four annual indices (rates of treatment, protocol adherence, in-time treatment, and complications) were recorded from 2009 to 2014 as outcome measures. The data were analyzed using the χ^2 test for significance.

Results The number of certified hospitals progressively increased from 74 to 112 during the 6-year period and finally consisted of 33 HD, 9 MoD and 70 MeD hospitals in 2014. The annual intravenous rtPA treatment rate increased significantly from 3.0% in 2009 to 4.5% in 2014. The protocol adherence rates were 95.7% in the HD group, 92.4% in the MoD group and 72.8% in the MeD group. The annual in-time treatment rate significantly improved from 26.0% in 2009 to 60.1% in 2014. The overall symptomatic intracranial hemorrhagic rate after rtPA treatment was 8.6%.

Conclusions Initiation of the HECAL-Stroke project by the government significantly improved rtPA treatment in Taiwan.

Keywords Ischemic stroke; Thrombolysis; Tissue-type plasminogen activator; Hospital Emergent Capability Accreditation by Level-Stroke; Taiwan Correspondence: Tsung-Hsi Wang Ministry of Health and Welfare, Executive Yuan, Republic of China, 10F, No. 488, Sec. 6, Zhongxiao E. Rd., Nangang Dist., Taipei City, 11558, Taiwan, Republic of China Tel: +886-2-85907750 Fax: +886-2-8590-7013 E-mail: Joyce12wang@gmail.com

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The authors have no conflicts of interest.

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Introduction

Stroke has been one of the top three causes of death and the most common cause of disability among adults in Taiwan over the past 30 years.^{1,2} The impact of the stroke-related medical and economic burdens on families and society is considerable. Therefore, the promotion of public awareness for the prevention of stroke and the optimization of treatments for patients with acute ischemic stroke (AIS) to minimize the overall burden of stroke-related dependency have become important health-care missions of the Ministry of Health and Welfare (MOHW), Executive Yuan, Republic of China.

Intravenous recombinant tissue plasminogen activator (IV rtPA) therapy within a limited time window (3 to 4.5 hours after stroke symptom onset) is the most important treatment with proven clinical efficacy and provides cost savings for select patients with AIS.^{3,4} Thrombolytic therapy with rtPA was approved for AIS in 2002 by the Taiwan Food and Drug Administration, and its efficacy has been thoroughly evaluated to improve the quality of stroke care in Taiwan.⁵ The Taiwan Stroke Registration program conducted by the Taiwan Stroke Society from 2006 to 2008 was the first nationwide effort in Taiwan to establish a reliable national stroke database to assess the guality of stroke care and to identify areas that required improvement. The study demonstrated that only 1.5% of patients with ischemic stroke and 8.8% of patients arriving at the hospital within 2 hours of stroke onset received IV rtPA treatment. The proportion of patients who received rtPA therapy in the Taiwan Stroke Registration was significantly lower than the proportion in the USA according to the Get With the Guidelines-Stroke study.6 However, increasing evidence has indicated that the establishment of primary stroke centers (PSCs) and certification by professionals is effective in increasing the use of rtPA therapy, which is regarded as an important measure of the quality of stroke care.7 Therefore, the nationwide project "Hospital Emergent Capability Accreditation by Level-Stroke (HECAL-Stroke)" launched by the MOHW in Taiwan in 2009 encouraged hospitals to establish a PSC and to set a standard requirement for PSC accreditation.8 The current study was to evaluate the impact of the nationwide HECAL-Stroke project on the improvement of IV rtPA treatment in Taiwan.

Methods

Hospital enrollment

HECAL is a nationwide hospital accreditation project launched by the MOHW in 2009 in Taiwan.⁸ The program evaluates six domains of hospital accreditation, including medical management in the emergency department, stroke, acute coronary syndrome, major trauma, gynecological and pediatric emergency, and intensive care unit. The evaluation process was conducted by an on-site peer reviewing committee according to the criteria of each domain from a nationwide consensus. The adequacies of the emergency department and intensive care unit facilities are basic requirements for participation in the nationwide hospital accreditation project. Initially, all participating hospitals were certified as "heavy duty (HD)" when they met all of the requirements for the acute management of stroke, acute coronary syndrome, major trauma, and gynecological and pediatric emergency and as "medium duty (MeD)" when they met only the requirement for the management of one of these conditions according to the audit results of the on-site peer review (initially and then every 4 years). In 2011, the additional certification "moderate duty (MoD)" was introduced to define a hospital meeting the requirements for the management of more than one of the conditions. In the current study, we enrolled all participating hospitals that met the HECAL criteria for acute stroke management in the HECAL-Stroke project to evaluate outcome measurements from 2009 to 2014.

Data collection

The performance of rtPA treatment was regarded as the major outcome measure for the HECAL-Stroke project. The participating and certified hospitals were requested to report annual data to the MOHW, including all six items listed below.

- 1. Number of patients with AIS
- 2. Number of patients with AIS arriving at the hospital within 3 hours who were eligible for IV rtPA treatment (Supplementary Methods 1)
- 3. Number of patients with AIS receiving IV rtPA treatment
- Number of patients with AIS who were eligible for rtPA therapy and received the treatment
- Number of patients with AIS who received IV rtPA treatment within 60 minutes of arrival at the emergency department
- 6. Number of symptomatic intracranial hemorrhage (SICH) events after rtPA therapy (SICH was defined as an intracranial hemorrhage detected on follow-up imaging and no less than 2 scales of deterioration according to the National Institutes of Health Stroke Scale within 36 hours after rtPA treatment)⁴

We assessed the following measures (A-D) as quality indicators:

A. Treatment rate, indicating the proportion of patients with AIS receiving rtPA therapy (calculated as the number of



Figure 1. Participating hospitals in the different levels from 2009 to 2014. HD, heavy duty; MeD, medium duty; MoD, moderate duty.

item 3 divided by the number of item 1 and then multiplied by 100%)

- B. Protocol adherence rate, indicating the proportion of patients with AIS who qualified for rtPA therapy and received the treatment (calculated as the number of item 4 divided by the number of item 2 and then multiplied by 100%)
- C. In-time treatment rate, indicating the proportion of patients with AIS who received IV rtPA treatment within 60 minutes (calculated as the number of item 5 divided by the number of item 3 and then multiplied by 100%)
- D. SICH rate, indicating the proportion of patients with SICH after IV rtPA therapy (calculated as the number of item 6 divided by the number of item 3 and then multiplied by 100%)

To achieve HECAL-Stroke accreditation, all hospitals must reach the minimal target goals within a four-year period, including a 1% treatment rate, 50% protocol adherence rate, and 30% in-time treatment rate every year.⁸

The study protocols were approved by the Institutional Review Board of Chi Mei Medical Center (approval No.: 10410-E07) for data analysis without personal patient identifiers.

Statistical analysis

All categorical variables were expressed as numbers and percentages, and the indices were presented as percentages. Pearson's χ^2 test or Fisher's exact test was used to analyze differences among two or three groups. All statistical tests were performed at the two-tailed significance level of 0.05. All data processing and statistical analyses were performed with the EXCEL[®] statistical software (Microsoft[®] Office 2010, Microsoft Corporation, Seattle, WA, USA).

Results

The number of certified hospitals increased from 74 in 2009 to 112 in 2014 and included 33 HD hospitals, 9 MoD hospitals and 70 MeD hospitals in 2013 and 2014 (Figure 1). Nearly all of the hospitals with the facilities to manage AIS patients in Taiwan were enrolled. Therefore, the study could reflect the findings of the nationwide project to improve acute stroke management for patients with AIS during the period from 2009 to 2014.

An estimated 31,000 patients experienced AIS yearly in Taiwan (Table 1). The four quality indicators were collected annually from the HD, MoD, and MeD summation data from 2009 to 2014 (Supplementary Table 1, Supplementary Figure 1). The annual IV rtPA treatment rate significantly increased from 3.0% in 2009 to 4.2% in 2011 and then gradually increased to 4.5% in 2014 (Table 1, Figure 2A). A comparison of the treatment rates among the three hospital levels showed that the highest rate was 5.7% in the MoD group, which was significantly higher compared to the other two groups (Table 2, Figure 3A).

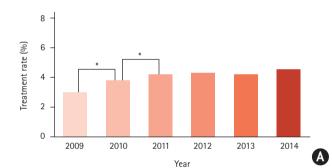
The overall protocol adherence rate was 87.1% (Table 1). The protocol adherence rates were 95.7% at the HD level, 92.4% at the MoD level and 72.8% at the MeD level, which represented significant differences (Table 2, Figure 3B). The annual protocol adherence rate was significantly lower in 2011(83.8%) than in 2010 (89.8%) and 2012 (86.8%) (Table 1, Figure 2B), which might be attributed to the poor protocol adherence, such as rtPA prescribed in patients older

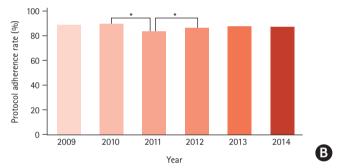
2009	2010	2011	2012	2013	2014	Total	Overall
74	80	100	111	112	112	NA	
12,481	16,905	26,707	31,558	31,499	30,771	149,921	
360	591	1,247	1,436	1,431	1,461	6,526	
377	640	1,121	1,350	1,328	1,370	6,186	
319	531	1,045	1,247	1,262	1,278	5,682	
98	242	559	747	778	823	3,247	
28	62	86	122	107	124	529	
3.0 [*]	3.8 ^{*,†}	4.2 ⁺	4.3	4.2	4.5		4.1
88.6	89.8 ⁺	83.8 ^{+,‡}	86.8 [§]	88.2	87.5		87.1
26.0 [*]	37.8 ^{*,+}	49.9 ^{+,‡}	55.3 [§]	58.6	60.1		52.5
7.4	9.7	7.7	9.0	8.1	9.1		8.6
	74 12,481 360 377 319 98 28 28 3.0 [°] 88.6 26.0 [°]	74 80 12,481 16,905 360 591 377 640 319 531 98 242 28 62 3.0° 3.8°* 88.6 89.8° 26.0° 37.8°*	74 80 100 12,481 16,905 26,707 360 591 1,247 377 640 1,121 319 531 1,045 98 242 559 28 62 86 3.0 [°] 3.8 ^{°,†} 4.2 [†] 88.6 89.8 [†] 83.8 ^{†,‡} 26.0 [°] 37.8 ^{°,‡} 49.9 ^{†,‡}	74 80 100 111 12,481 16,905 26,707 31,558 360 591 1,247 1,436 377 640 1,121 1,350 319 531 1,045 1,247 98 242 559 747 28 62 86 122 3.0° 3.8°* 4.2° 4.3 88.6 89.8° 83.8°* 86.8° 26.0° 37.8°* 49.9°* 55.3°	74 80 100 111 112 $12,481$ $16,905$ $26,707$ $31,558$ $31,499$ 360 591 $1,247$ $1,436$ $1,431$ 377 640 $1,121$ $1,350$ $1,328$ 319 531 $1,045$ $1,247$ $1,262$ 98 242 559 747 778 28 62 86 122 107 $3.0^{'}$ $3.8^{',+}$ 4.2^{+} 4.3 4.2 88.6 89.8^{\dagger} $83.8^{\dagger,+}$ 86.8^{5} 88.2 $26.0^{'}$ $37.8^{',+}$ $49.9^{\dagger,+}$ 55.3^{5} 58.6	7480100111112112 $12,481$ $16,905$ $26,707$ $31,558$ $31,499$ $30,771$ 360 591 $1,247$ $1,436$ $1,431$ $1,461$ 377 640 $1,121$ $1,350$ $1,328$ $1,370$ 319 531 $1,045$ $1,247$ $1,262$ $1,278$ 98 242 559 747 778 823 28 62 86 122 107 124	74 80 100 111 112 112 NA 12,481 16,905 26,707 31,558 31,499 30,771 149,921 360 591 1,247 1,436 1,431 1,461 6,526 377 640 1,121 1,350 1,328 1,370 6,186 319 531 1,045 1,247 1,262 1,278 5,682 98 242 559 747 778 823 3,247 28 62 86 122 107 124 529 3.0° 3.8°* 4.2* 4.3 4.2 4.5 88.6 89.8* 83.8** 86.8* 88.2 87.5 26.0° 37.8°* 49.9** 55.3* 58.6 60.1

Table 1. Annual data and indicators for AIS patients receiving rtPA therapy from 2009 to 2014 in the project "Hospital Emergent Capability Accreditation by Level-Stroke"

AIS, acute ischemic stroke; rtPA, recombinant tissue plasminogen activator; no., number; NA, not applicable; min., minutes; SICH, symptomatic intracranial hemorrhage.

P<0.05, 2009 vs. 2010; P<0.05, 2010 vs. 2011; P<0.05, 2011 vs. 2012. Significant differences between the two groups of the index were analyzed with a χ^2 test with P<0.05.





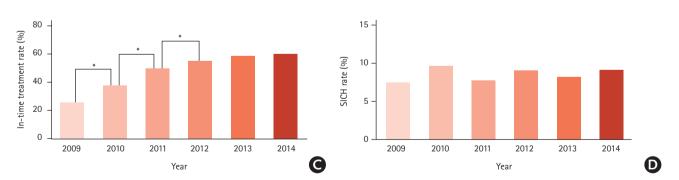


Figure 2. Annual indicators for AIS patients receiving rtPA therapy from 2009 to 2014 in the project of "Hospital Emergent Capability Accreditation by Level-Stroke." (A) Treatment rate, (B) protocol adherence rate, (C) in-time treatment rate, and (D) SICH rate. AIS, acute ischemic stroke; rtPA, recombinant tissue plasminogen activator; SICH, symptomatic intracranial hemorrhage. *Represents a significant difference between groups analyzed with a χ^2 test with *P*<0.05.

than 80 years old or 3–4.5 hours of AIS onset, in the MeD group (Table 2, Figure 3B, Supplementary Table 1, Supplementary Figure 1B).

The annual in-time rates significantly improved from 26.0%

in 2009 (24.5% in the HD group and 34.5% in the MeD group) to 55.3% in 2012 and then gradually improved to 60.1% (57.5% in the HD group, 61.2% in the MoD group and 63.6% in the MeD group) in 2014 (Table 1, Figure 2C, Supplementary

Table 2. Data and indicators for AIS patients receiving rtPA therapy at different hospital levels from 2009 to 2014 in the project of "Hospital Emergent Capability Accreditation by Level-Stroke"

	HD	MoD	MeD	Total	Overall
Items					
1. AIS	94,354 (62.9)	7,479 (5.0)	48,088 (32.1)	149,921	
2. Eligible for rtPA	3,729 (57.1)	396 (6.1)	2,401 (36.8)	6,526	
3. rtPA administration	3,973 (64.2)	430 (7.0)	1,783 (28.8)	6,186	
4. Qualifying for rtPA criteria	3,567 (62.8)	366 (6.4)	1,749 (30.8)	5,682	
5. Administration of rtPA within 60 min.	2,033 (62.6)	241 (7.4)	973 (30.0)	3,247	
6. SICH	229 (43.3)	22 (4.2)	278 (52.6)	529	
Indicator (item no./item no.) (%)					
Treatment rate (3/1)*	4.2 ^{+,+}	5.7 ^{+,§}	3.7 ^{‡,§}		4.1
Protocol adherence rate (4/2) ⁺	95.7 ^{‡,§}	92.4 ^{‡,II}	72.8 ^{§,II}		87.1
In-time treatment rate (5/3) ⁺	51.2 [§]	56.0	54.6 [§]		52.5
SICH rate (6/3) ⁺	5.8 ^{\$}	5.1 [#]	15.6 ^{₅,}		8.6

Values are presented as n (%) unless otherwise indicated.

AIS, acute ischemic stroke; HD, heavy duty; MeD medium duty; MoD, moderate duty; min., minutes; rtPA, recombinant tissue plasminogen activator; SICH, symptomatic intracranial hemorrhage.

*Significant differences between two groups of the index analyzed with a χ^2 test with *P*<0.05; [†]P<0.05 HD vs. MeD; [†]*P*<0.05 HD vs. MoD; [§]*P*<0.05 HD vs. MeD; [§]

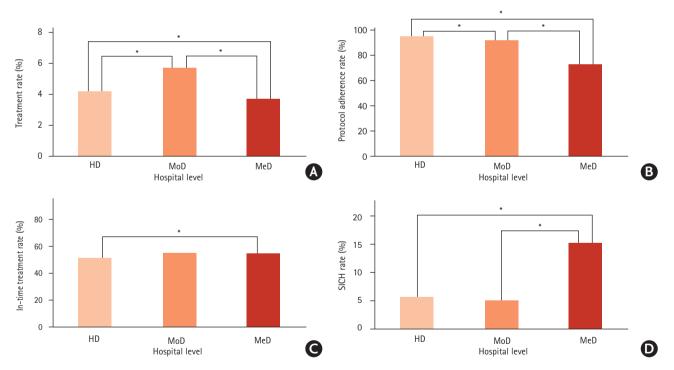


Figure 3. Indicators for AIS patients receiving rtPA therapy at different hospital levels from 2009 to 2014 in the project of "Hospital Emergent Capability Accreditation by Level-Stroke". (A) Treatment rate, (B) protocol adherence rate, (C) in-time treatment rate, and (D) SICH rate. AIS, ischemic stroke; HD, heavy duty; MeD medium duty; MoD, moderate duty; rtPA, recombinant tissue plasminogen activator; SICH, symptomatic intracranial hemorrhage. *Represents a significant difference between groups analyzed with P < 0.05.

Table 1, Supplementary Figure 1C). The overall in-time treatment rates were 51.2% at the HD level and 54.6% at the MeD level, which represented significant difference (Table 2, Figure 3C).

The overall complication rate after IV rtPA treatment was 8.6%, and no significant differences were detected between the years (Table 1, Figure 2D). However, the differences in the

complication rates were significant, with the highest rate of 15.6% observed in the MeD group, followed by 5.8% in the HD group and 5.1% in the MoD group (Table 2, Figure 3D).

Discussion

A previous study demonstrated that only 1.5% of patients with AIS received IV rtPA treatment between 2006 and 2008 in Taiwan.⁵ This study demonstrated that the HECAL-Stroke project launched by the MOHW of Taiwan significantly increased the rtPA treatment rate in patients with AIS from 3.0% in 2009 to 4.5% in 2014. Accordingly, the in-time rate of rtPA treatment also significantly increased in all groups (HD, MoD and MeD) from 2009 to 2014. The overall complication rate was 8.6% in the rtPA-treated patients at all hospital levels, but no significant differences were detected between 2009 and 2014.

Increasing evidence has indicated that the implementation and certification of a PSC may improve the clinical performance of rtPA treatment in AIS patients.^{9,10} Prior to PSC certification, Kleindorfer et al. found that the rtPA treatment rate was extremely low (approximately 1.8–2.1% of AIS patients) in both the Medicare Provider Analysis and Review database and the Premier Hospital database between 2001 and 2004.¹¹ The treatment rate was significantly higher in PSC-certified hospitals by the Joint Commission on Accreditation of Healthcare Organizations than in uncertified hospitals (5.0% versus 1.4%) in 2010.¹² Interestingly, Lattimore et al. reported that the establishment of a PSC at a community hospital resulted in a substantial increase in the proportion of AIS patients receiving rtPA therapy, from 1.5% before certification to 10.5% 2 years after certification.⁷

Earlier evidences inspired the MOHW of Taiwan for launching the project of HECAL-Stoke. The current study indicated that the treatment rate significantly increased not only in the MeD group, which primarily consists of community hospitals, but also in the HD group with academic medical centers. This finding suggests that Taiwan's HECAL-Stroke project for the certification of PSCs was effective in increasing the rtPA treatment rate for AIS patients in both community hospitals and academic medical centers. In addition to increasing the rtPA treatment rate for AIS patients, Taiwan's HECAL-Stroke project significantly increased the in-time treatment rate from 26.0% in 2009 to 60.1% in 2014 (Table 1) compared with the in-time treatment rate of 8.8% from 2006 to 2008 in Taiwan.⁵ This result may indicate that the process of AIS evaluation and treatment changed at many levels after the initiation of Taiwan's HECAL-Stroke project for stroke certification, which facilitated community hospitals and academic medical centers to standardize numerous aspects of stroke care. It could be the main reason for increasing rtPA treatment rate.

The hospitals that did not meet the criteria for stroke centers were not recruited for treatment quality data in the study. Although all hospitals met the criteria for acute stroke management, there were the disparities of treatment outcomes among the stroke centers. The differences of treatment outcomes may be related to patients' demographics and the various levels of hospital designation for stroke care, which includes human and structural resources and integrated pathways for management of acute stroke patients. The MoD hospitals had the significantly highest treatment rate than the HD and MeD hospitals, but had no higher in-time treatment and protocol adherence rates than the HD hospitals. The reason may be ascribed to the fact that the MoD hospitals are regional and convenient for stroke patients with reduction of prehospital delay. Further exploring the contributors for the disparities of treatment outcomes among various levels of stroke center is needed in the future.

Based on previous evidence, a shorter onset-to-treatment time leads to a better prognosis in AIS patients.¹³ Lindsberg et al. streamlined the triage process in the emergency room (ER) to reduce the onset-to-treatment time and thereby reduced in-hospital delays and enhanced thrombolysis access for AIS patients.13 Saver et al. also found that every 15-minute increment of a faster onset-to-treatment time was associated with reduced in-hospital mortality, reduced SICH, increased independent ambulation at discharge, and increased discharge to home.¹⁴ Unfortunately, although the Taiwan HECAL-Stroke project was effective for increasing the in-time treatment rate, the overall SICH rate was 8.6%, which was higher than the rates of 6.7% reported in the NINDS rtPA trial⁴ and 7.7% in a meta-analysis of rtPA treatment in AIS patients.¹⁵ Previous reports from Albers et al. indicated that the SICH rate was 3.3% when 32.6% of the treated patients violated treatment protocols,¹⁶ and Katzan et al. found that the SICH rate increased to 15.7% when 50% of the treated patients violated the rtPA treatment protocol criteria.¹⁷ The higher SICH rate in the study may be attributed to poorer protocol adherence because the overall protocol adherence rate was 87.1%. Additionally, the MeD group had the lowest protocol adherence rate but the highest SICH rate compared to the HD and MoD groups. For the limited data reported to MOHW only with an item of adherence or not rather than detailed information, future study is worthy to explore the factors associated with SICH rate to find out these interesting clinical issues.

Through the efforts of Taiwan's HECAL-Stroke accreditation, the treatment rate increased from 3.0% to 4.5% and the in-

time treatment rate increased from 26% to 60.1% from 2009 to 2014. However, the American Heart Association's Get With the Guidelines-Stroke study demonstrated that rtPA treatment less than 3 hours after stroke onset increased from 4.0% to 7.0% for all AIS patients and from 42.6% to 77.0% in AIS patients arriving at the hospital ≤ 2 hours after stroke onset from 2003 to 2011.6 The HECAL-Stroke project clearly shows that there is still room for improvement in rtPA therapy among Taiwan's AIS patients. According to the stroke chain of survival recommended by the 2013 American Stroke Guidelines,18 shortening onset to ER arrival and door to needle time intervals are helpful to improve the rate of thrombolytic therapy for AIS. A previous study in Taiwan also indicated that the time interval between symptom onset and the decision to call for medical care was far from optimal and was the underlying cause of prolonged prehospital delay.¹⁹ Another study demonstrated that a new designed program with video-assisted therapeutic risk communication significantly decreased the door-to-needle time and increased the percentage of rtPA thrombolytic therapy in patients with AIS.²⁰ However, the study did not include the data of onset to ER arrival and door to needle time intervals. Recently, several strategies have been proposed by the MOHW of Taiwan to continually improve access to IV rtPA and to increase the proportion of patients receiving the treatment. At the beginning of 2016, the MOHW of Taiwan began to pay for rtPA treatment to increase financial incentives for hospitals aiming to improve their rtPA administration rates. Additionally, several strategies for the implementation of stroke treatment have been undertaken by the MOHW of Taiwan, such as adding a new indicators "the rate of door to needle time less than 60 minutes" as outcome indicator in HECAL-Stroke project, streamlining pre-hospital stroke management, setting up a telemedicine consulting network for acute stroke management, and processing the approval of mechanical thrombectomy by Taiwan Food and Drug Administration for acute stroke patients with large artery occlusion.

The strength of this study is that this was a nationwide project initiated by the government first for the setting of PSC in Taiwan. However, several limitations should be considered when interpreting the study results. First, the outcome measures were related to rtPA treatment, which might have been affected by the denominator and eligibility criteria when the calculations were performed to detect significant differences. Second, the influence of other stroke public awareness campaigns might have contributed to the improvement of stroke therapy during the study period. Third, the variability in factors explored across different levels of hospital care, such as the interaction between the cause of protocol violation for rtPA treatment and the severity of SICH, was not considered and might have introduced some bias into the study. The development of a broad and detailed framework that can be applied to future studies in this area may be useful.

Conclusions

The "HECAL-Stroke" project from the MOHW of Taiwan significantly improved rtPA treatment in AIS patients in Taiwan. These findings indicate that a thoughtfully designed and wellreported project initiated by the government to improve stroke treatment quality can be effective in both academic medical centers and community hospital settings. However, the implementation of stroke healthcare not only includes rtPA treatment but also lifestyle modifications, risk factor management,^{21,22} secondary stroke prevention and post-stroke care, and the development of systems such as telestroke and mechanical thrombectomy. Therefore, the integration of stroke services in the future will remain a great challenge for the MOHW of Taiwan.

Supplementary Materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2016.01655.

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Supplementary Methods 1. Criteria for IV rtPA therapy by National Health Insurance in Taiwan.

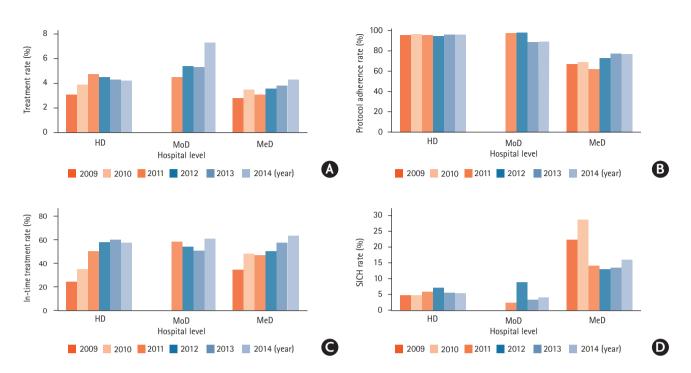
Inclusion criteria:

- 1. Age between 18 and 80 years old
- 2. Non-contrast computed tomography (CT) scan showing no hemorrhage
- 3. Acute ischemic stroke with symptoms onset less than 3 hours and complete evaluation

Exclusion criteria:

- 1. Acute ischemic stroke with symptoms onset more than 3 hours or unknown
- 2. Rapid improvement of stroke symptoms or stroke severity too mild (the National Institutes of Health Stroke Scale [NIHSS] less than 6)
- 3. Stroke severity too severe (NIHSS greater than 25) or hypodensity greater than 1/3 cerebral hemisphere on CT findings
- 4. Seizure at onset
- 5. Recent head trauma, or stroke (less than 3 months)
- 6. History of stroke with Diabetes mellitus
- 7. Heparin used in 48 hours before stroke and prolonged aPTT
- 8. Platelets less than 100,000/mm3
- 9. Active internal bleeding
- 10. Intracranial brain tumor or brain aneurysm or vascular malformation
- 11. Systolic blood pressure greater than 185 or diastolic blood pressure greater than 110 mm Hg or needed to be aggressively treated by IV medication to reach these target levels
- 12. Glucose less than 50 or greater than 400 mg/dL
- 13. Patients currently receiving oral anticoagulant, such as Warfarin sodium with PT INR>1.3
- 14. History of intracranial hemorrhage or brain aneurysm or vascular malformation or brain tumor, intracranial or spinal surgery
- 15. History, suspicion or approval of intracranial hemorrhage, subarachnoid hemorrhage
- 16. Serious and uncontrolled hypertension
- 17. Recent surgery, serious trauma or head injury (less than 10 days) including acute myocardia infarct
- 18. Prolonged or traumatic cardiopulmonary cerebral resuscitation (more than 2 minutes), delivery, recent (less than 10 days) uncompressible vascular puncture (such as subclavian or neck central venous puncture)
- 19. Severe hepatic diseases, including hepatic failure, liver cirrhosis, portal hypertension (esophageal varicose vein), and acute hepatitis
- 20. Hemorrhagic retinopathy (such as diabetic), or other hemorrhagic ophthalmic conditions
- 21. Subacute bacterial endocarditis, acute pericarditis
- 22. Acute pancreatitis
- 23. Peptic ulcer disease in recent 3 months
- 24. Aneurysm, arteriovenous malformation
- 25. Tumor with easy bleeding
- 26. Allergy to rt-PA or adjuvant agent
- 27. Other conditions with increased risk of bleeding, such as hemodialysis, heart failure, cachexia

Hospital level			ЧD						MoD	Q					MeD			
Year	2009	2010	2011	2012	2013	2014	2009	2010	2011	2012	2013	2014	2009	2010	2011	2012	2013	2014
Hospital no.	27	28	31	33	33	33	•,	ı	7	ω	6	6	47	52	62	70	70	70
ltems																		
1. AIS	10,440	10,440 13,061	17,207	18,460	17,696	17,490	ī	ı	912	2,305	2,235	2,027	2,041	3,844	8,588	10,793	11,568	11,254
2. Eligible for rtPA	274	449	760	797	749	700	ı	ı	43	110	115	128	86	142	444	529	567	633
3. rtPA administration	319	507	810	834	769	734	ı	ı	41	124	118	147	28	133	270	392	441	489
4. Qualifying for rtPA criteria	261	433	725	754	719	675	ı	ı	42	108	102	114	28	98	278	385	441	489
5. Administration of rtPA within 60 min.	78	178	408	483	464	422	ı	ı	24	67	09	06	20	64	127	197	254	311
6. SICH	15	24	47	60	43	40	ı	ı	-	11	4	9	13	38	38	51	60	78
Indicator (item no./item no.) (%)																		
Treatment rate (3/1)	3.1	3.9	4.7	4.5	4.3	4.2	ı	ı	4.5	5.4	5.3	7.3	2.8	3.5	3.1	3.6	3.8	4.3
Protocol adherence rate (4/2)	95.3	96.4	95.4	94.6	96.0	96.4	ı	ı	97.7	98.2	88.7	89.1	67.4	69.0	62.6	72.8	77.8	77.3
In-time treatment rate (5/3)	24.5	35.1	50.4	57.9	60.3	57.5	ı	ı	58.5	54.0	50.8	61.2	34.5	48.1	47.0	50.3	57.6	63.6
SICH rate (6/3)	4.7	4	5.8	7.2	5.6	5.4	ī	I	2.4	8.9	3.4	4.1	22.4	28.6	14.1	13.0	13.6	16.0



Supplementary Figure 1. Annual indices for AIS patients receiving rtPA therapy at different hospital levels from 2009 to 2014 in the project "Hospital Emergent Capability Accreditation by Level-Stroke". (A)Treatment rate, (B) protocol adherence rate, (C) in-time treatment rate, and (D) SICH rate. AIS, acute ischemic stroke; rtPA, recombinant tissue plasminogen activator; HD, heavy duty; MoD, moderate duty; MeD medium duty; SICH, symptomatic intracranial hemorrhage.

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