Stroke

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Associations Between Adherence to Evidence-Based, Stroke Quality Indicators and Outcomes of Acute Reperfusion Therapy

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BACKGROUND: Quality indicators (QIs) are an accepted tool for measuring a hospital's performance in routine care. We examined national trends in adherence to the QIs developed by the Close The Gap-Stroke program by combining data from the health insurance claims database and electronic medical records, and the association between adherence to these QIs and early outcomes in patients with acute ischemic stroke in Japan.

METHODS: In the present study, patients with acute ischemic stroke who received acute reperfusion therapy in 351 Close The Gap-Stroke-participating hospitals were analyzed retrospectively. The primary outcomes were changes in trends for adherence to the defined QIs by difference-in-difference analysis and the effects of adherence to distinct QIs on in-hospital outcomes at the individual level. A mixed logistic regression model was adjusted for patient and hospital characteristics (eg, age, sex, number of beds) and hospital units as random effects.

RESULTS: Between 2013 and 2017, 21 651 patients (median age, 77 years; 43.0% female) were assessed. Of the 25 defined measures, marked and sustainable improvement in the adherence rates was observed for door-to-needle time, door-to-puncture time, proper use of endovascular thrombectomy, and successful revascularization. The in-hospital mortality rate was 11.6%. Adherence to 14 QIs lowered the odds of in-hospital mortality (odds ratio [95% CI], door-to-needle <60 min, 0.80 [0.69–0.93], door-to-puncture <90 min, 0.80 [0.67–0.96], successful revascularization, 0.40 [0.34–0.48]), and adherence to 11 QIs increased the odds of functional independence (modified Rankin Scale score 0–2) at discharge.

CONCLUSIONS: We demonstrated national marked and sustainable improvement in adherence to door-to-needle time, door-to-puncture time, and successful reperfusion from 2013 to 2017 in Japan in patients with acute ischemic stroke. Adhering to the key QIs substantially affected in-hospital outcomes, underlining the importance of monitoring the quality of care using evidence-based QIs and the nationwide Close The Gap-Stroke program.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: ischemic stroke ■ mortality ■ quality indicator ■ reperfusion ■ thrombectomy

There is substantial evidence regarding effective strategies for stroke treatment, management, and prevention that have been translated into several international and national clinical guidelines.[1,2] Quality indicators (QIs) are widely used tools for measuring the performance of individual hospitals in delivering

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Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
CSC	comprehensive stroke center
CTGS	Close The Gap-Stroke
DTN	door-to-needle
DTP	door-to-puncture
DTVI	door-to-intracranial vascular imaging
DVT	deep venous thrombosis
EVT	endovascular thrombectomy
NIHSS	National Institutes of Health Stroke Scale
PSC	primary stroke center
QI	quality indicator
r-tPA	recombinant tissue-type plasminogen activators

appropriate stroke care. There are several initiatives in Europe and the United States to define QIs in a standardized, evidence-based way for national implementation.[3,4]

The J-ASPECT study (a nationwide survey of Acute Stroke Care Capacity for Proper Designation of Comprehensive Stroke Center in Japan) was launched in 2010 as the first nationwide survey of acute stroke clinical practices using data from the Japanese health insurance claims database.[5] The J-ASPECT study group further launched the Close The Gap-Stroke (CTGS) program, the first nationwide quality improvement initiative in Japan, to develop standardized QIs for primary stroke centers (PSCs) and comprehensive stroke centers (CSCs).[6] This program developed a QI measuring tool by combining data from electronic medical records and the health insurance claim database to reduce the burden on physicians and medical information managers in participating hospitals.[7] Using this novel approach, our previous study conducted in 2017 demonstrated that all target QIs for acute ischemic stroke (AIS) were successfully obtained with minimal missing data from 8206 patients treated with intravenous r-tPA (recombinant tissue-type plasminogen activators) or endovascular thrombectomy (EVT) from 172 hospitals between 2013 and 2015.[7] Pivotal trials for AIS in 2015 established EVT as the standard care for patients with large vessel occlusion-related AIS.[8] However, national trends regarding the adherence to the defined QIs in stroke centers in response to such paradigm shift remain unclear. Thus, we conducted the second CTGS survey in 2020 to compare national trends in the QI adherence before and after the publication of the pivotal trial.[8]

Furthermore, uncertainty exists about whether quality improvement strategies translate into better patient outcomes.[9,10] The data regarding the association between QI adherence and patient outcomes are inconsistent, ranging from a positive relationship to no relationship between increased adherence to process measures and patient outcome.[9–12] We explored the association between the quality of acute stroke care measured by the CTGS program[7] and the clinical outcomes at discharge, defined as in-hospital death and functional independence (modified Rankin Scale score of 0–2).

METHODS

Participation in the CTGS program in the J-ASPECT study was voluntary and undertaken in collaboration with the Japan Neurosurgical Society and the Japan Stroke Society.[5,13] The PSCs in Japan were encouraged to participate in the J-ASPECT study and the CTGS program in Japan as part of the 5-year plan to conquer stroke and cardiovascular diseases by the Japan Neurosurgical Society and Japan Stroke Society. The data that support the findings of this study are available from the corresponding author upon reasonable request. The manuscript was prepared in accordance with the RECORD (The Reporting of Studies Conducted Using Observational Routinely Collected Health Data) reporting guidelines.[14]

In this study, we retrospectively identified 32 915 AIS patients who received r-tPA infusion or EVT from January 2013 to December 2017 from the Diagnosis Procedure Combination claim database of 610 hospitals participating in the J-ASPECT Study[5,13]; patients aged <18 years on admission were excluded (Figure 1). Among these hospitals, 421 hospitals (22 310 patients) agreed to participate in the CTGS program. After 6352 patients were excluded due to incomplete data (5732 patients) and low hospital case volume (<5 per year) of r-tPA or EVT (620 patients in 69 hospitals), 21 651 patients with AIS from 351 hospitals were included in the final dataset.

CTGS QIs and Measurement Tool

Details of the CTGS and evidence-based QIs have been published previously.[6,7] In brief, 17 QIs for PSCs reflect basic stroke care, whereas 12 QIs for CSCs reflect advanced stroke care (Table S1). Of the 29 QIs in total, 4 related to subarachnoid hemorrhage and nontraumatic intracerebral hemorrhage for CSCs (indicators 8–11) were excluded; only QIs relevant to AIS were selected for this study. The selected QIs evaluated diagnosis (PSC 1–4 and CSC 1), acute medications and procedures (PSC 6–8 and CSC 2–4), initiation of secondary preventive treatments (PSC 9–12), multidisciplinary team care and prevention of complications (PSC 5, 13–15), patient education (PSC 16, 17), and post-discharge assessment (CSC 7). Symptomatic intracranial hemorrhage (CSC 6) and stroke or death within 24 hours of diagnostic angiography (CSC 12) were used to evaluate safety measures. Some QIs are time metrics (PSC 2, 7 and CSC 1, 5) and intermediary outcome measures (CSC 4). Time intervals for the door-to-intracranial vascular imaging (DTVI) time and the door-to-puncture (DTP) time were set at 30 and 140 minutes, respectively, according to the QIs for EVT.[15] Two additional time intervals (60 and 90 minutes) for DTP were also added.[16]

The CTGS measurement tool was developed to efficiently measure QIs by combining data from electronic medical records and the health insurance claim database.[7] The research office set relevant data (60% of the data to calculate 25 QIs)

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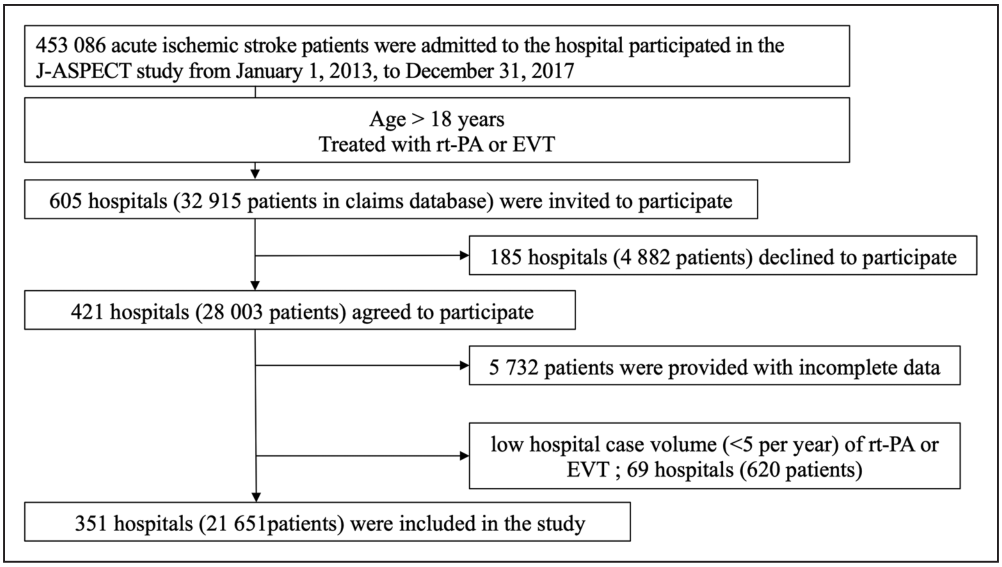

Figure 1. Inclusion criteria flow chart.

EVT indicates endovascular thrombectomy; J-ASPECT study, A Nationwide Survey of Acute Stroke Care Capacity for Proper Designation of Comprehensive Stroke Center in Japan; and r-tPA, recombinant tissue-type plasminogen activators.

from the Diagnosis Procedure Combination database in the CTGS tool, and sent this tool to the participating hospitals. The responsive physicians (the CTGS collaborators) in those hospitals were asked to review the preset data and add necessary information (eg, the National Institutes of Health Stroke Scale [NIHSS] score, door-to-needle [DTN] time, etc) from the electronic medical records. The completed dataset was then returned to the research office for cleaning data (eg, removing duplicates, erasing incomplete data, etc).[7] Adherence to each QI was calculated at the individual patient level.

Ethics Statement

This study was approved by the National Cerebral and Cardiovascular Center Institutional Review Board (R20058-2), which waived the requirement for informed consent from the participants.

Statistical Analyses

The primary outcomes were trends in adherence rates to the defined QIs over the study period, and the effects of adherence on death and functional independence at discharge on an individual level. All continuous variables are presented as medians (interquartile range). Noncontinuous and categorical variables are presented as frequencies or percentages. Changes in categorical variables were evaluated using the Cochran-Armitage test for trends, and changes in continuous variables were evaluated using the Jonckheere-Terpstra test for trends. We used a mixed logistic regression model using hospital units as a random effect to investigate trends in adherence to the QIs before and after the publication of the 2015 EVT trial; these are expressed by odds ratios (ORs) of adherence to the QIs per year and their 95% CIs. Additionally, we reported difference-in-difference estimates of adherence per year using ORs and 95% CIs. As for the assessments of QI and clinical outcomes, ORs and 95% CIs were calculated using a mixed logistic regression model adjusted for patient characteristics (eg, age, sex, and severity at admission measured by the NIHSS), comorbidities (eg, hypertension, diabetes, hyperlipidemia, atrial fibrillation, smoking status, and all AIS subtypes), and hospital characteristics (eg, the number of beds, annual stroke discharge, teaching status, and geographic factors categorized by location according to the 2015 governmental population density data) as fixed effects and hospital units as random effect. Each measure for which a patient was eligible contributed an observation in this analysis, and the outcome was a dichotomized variable indicating whether the care opportunity was fulfilled.[1] This study did not analyze the effect of adherence to QIs related to secondary preventive measures (eg, discharge on antiplatelet or anticoagulation medication) on in-hospital outcomes at discharge. For the safety measures, avoiding complications, not the occurrence, was assessed.

All statistical analyses were conducted using STATA 15 (StataCorp, College Station, TX). All statistical analyses were 2-tailed, and statistical significance was set at $P<0.05$.

RESULTS

Trends in Patient and Hospital Characteristics

Table presents the patient demographics and clinical outcomes in the final dataset. The median age was 77 years (interquartile range, 68–84), 43.0% were female, ≈60% had a cardioembolic stroke, the median NIHSS score was 14 (interquartile range, 7–21), and 78.5% and 42.8% of patients received r-tPA and EVT, respectively. Of those enrolled, functional independence was achieved in 37.9% and 47.8% at discharge and at 90 days, respectively. These patients were older, less likely to be atherothrombotic, hypertensive, and have severe stroke, and were more likely to receive EVT than those excluded due to low hospital case volume (Table S3).

Over the study period, the proportion of women, lacunar infarction, patients with any comorbidity, and those using anticoagulation medication before hospitalization increased (Table). The proportion of patients receiving r-tPA decreased, whereas those receiving EVT with or without r-tPA increased. Despite no considerable change in stroke severity, the proportion of deaths at discharge (from 10.1%–8.5%) and 90-day mortality (from 18.8%–15.8%) decreased, but the proportion of patients with functional independence at discharge or 90-day follow-up did not change.

Temporal Changes in the CTGS QIs From 2010 to 2017

Of the 25 defined measures compared with 2013 baseline levels, 5 QIs (DTN time <60 min, proper use of EVT, DTP time <90 min, DTP time <60 min, and successful revascularization after EVT) showed marked improvement in 2017. Furthermore, 2 QI measures (dysphagia screening and early rehabilitation) demonstrated a moderate increase in adherence in 2017. Figure 2 illustrates ORs of adherence to the individual CTGS QIs by year during the study period before and after 2015, and compares the changes in trends in adherence by year between before and after 2015.

The QIs were classified into 4 groups according to ORs of adherence to the QI by year before and after 2015. Among 25 QIs, ORs of adherence to 6 QIs by year were significant both before and after 2015 (eg, NIHSS documentation, DTP time, successful reperfusion, etc), and 3 of them (eg, DTP time <60 min, etc) showed significant changes in trends in adherence between before and after 2015. As for 12 QIs (eg,

Table. Characteristics of Patients in the Close The Gap-Stroke Program

Patient characteristics (n=21 651)	Overall	2013 (n=2137)	2014 (n=2777)	2015 (n=3730)	2016 (n=5712)	2017 (n=7295)	5 y Trend *P*
Demographics							
Age, y*	77 (68–84)	76 (67–83)	77 (68–83)	77 (68–84)	77 (68–84)	77 (69–84)	<0.0001†
Female gender	43.0	41.0	42.7	42.3	42.1	44.7	0.0032†
Stroke subtype							
Atherothrombotic	23.5	23.6	25.0	23.0	24.1	22.7	0.0609
Cardioembolic	60.2	60.6	60.7	61.1	59.3	60.2	0.2382
Lacunar	4.3	3.9	3.4	4.5	4.2	4.6	0.031†
Others or unknown	12.1	11.8	10.9	11.5	12.4	12.6	0.0048†
Comorbidity							
Hypertension	53.5	51.8	52.3	52.1	54.8	54.1	0.0062†
Diabetes	19.9	18.7	18.2	19.5	21.0	20.2	0.0072†
Hyperlipidemia	24.2	22.2	21.8	22.6	25.0	26.0	<0.0001†
Atrial Fibrillation	43.7	41.3	41.1	40.6	44.4	46.5	<0.0001†
Current smoking	16.8	17.1	16.9	16.7	17.8	16.0	0.2943
NIHSS scores on admission*	14 (7–21)	14 (8–21)	14 (7–20)	14 (7–21)	14 (7–20)	14 (7–21)	0.905
Treatment							
IV r-tPA only	56.3	75.3	66.5	57.5	55.1	47.1	<0.0001†
EVT only	21.4	11.1	15.7	20.2	21.8	27.0	<0.0001†
IV r-tPA+EVT	22.3	13.6	17.8	22.3	23.1	26.0	<0.0001†
Successful recanalization	76.1	62.0	71.5	78.5	79.9	80.7	<0.0001†
Hospitalization days*	23 (14–37)	24 (14–40)	24 (14–39)	23 (14–39)	22 (14–37)	23 (14–36)	0.0021†
Clinical outcomes							
In-hospital death	8.8	10.1	9.6	8.8	8.4	8.5	0.0077†
90-day mortality (n=13 821)	16.3	18.8	17.9	16.4	15.2	15.8	0.0014†
Functional independence (mRS score 0–2)							
At discharge	37.9	37.6	36.9	39.5	38.5	37.1	0.6304
At 90 days after discharge (n=13 707)	47.8	47.7	44.2	48.9	48.9	48.1	0.0907

The values are expressed as percentages unless otherwise indicated. Significance was assessed using the Cochran-Armitage test for categorical outcomes and the Jonckheere-Terpstra test for continuous outcomes. EVT indicates endovascular thrombectomy; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and r-tPA, recombinant tissue-type plasminogen activators.

*Median (interquartile range).

†Significant differences (P<0.05).

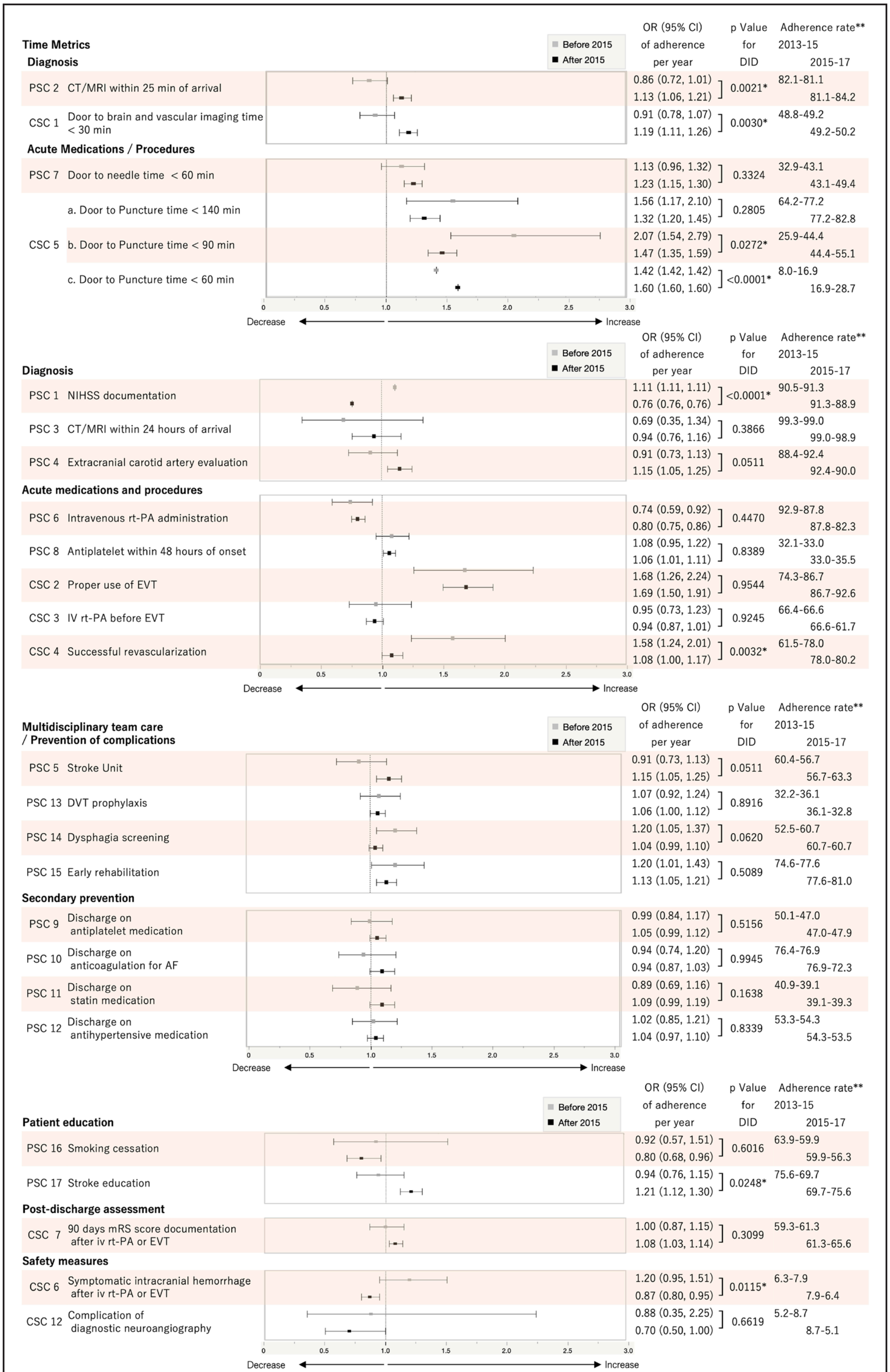

Figure 2. The Close The Gap-Stroke program quality indicators and change of trend before and after 2015.
Odds ratios (ORs) and 95% CIs for the change in trend of adherence were calculated using a mixed logistic regression model and hospital units as a random effect. The estimated OR and 95% CI of change in trend per year is represented by the squares and horizontal lines, respectively. Open and closed squares represent before and after the publication of the 2015 EVT trial, respectively. CSC indicates comprehensive stroke centers; CT, computed tomography; DID, difference-in-difference; DVT, deep vein thrombosis; EVT, endovascular thrombectomy; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PSCs, primary stroke centers; and r-tPA, recombinant tissue-type plasminogen activators. *Significant difference in DID analysis (P<0.05). **Overall adherence rates at the individual level are listed.

DTN time, DTVI time, symptomatic intracranial hemorrhage after r-tPA or EVT, stroke unit care, etc), ORs of adherence by year were significant only after 2015, and 4 QIs of them (eg, DTN time, DTVI time, etc) demonstrated significant change in trends in adherence between before and after 2015. As for dysphagia screening, OR of adherence by year were significant only before 2015, and no change of trends in adherence between before and after 2015 was observed. Regarding the remaining 6 QIs (eg, computed tomography/magnetic resonance imaging within 24 hours of arrival, IV r-tPA before EVT, etc), there were no significant changes in trends in adherence both before and after 2015.

Overall, 7 QIs demonstrated significant changes in trends in adherence between before and after 2015. Compared with ORs of adherence per year before 2015, ORs per year after 2015 was significantly larger in 4 QIs, mainly related to time metrics, but smaller in 3 QIs (eg, NIHSS score documentation, successful recanalization, symptomatic intracranial hemorrhage after r-tPA or EVT).

Associations Between QI Adherence and Clinical Outcomes

Figure 3 presents the associations between QI adherence and clinical outcomes at the patient level. Five time-associated QIs (DTI time <25 min, DTVI time <30 min, DTN time <60 min, DTP time <140 and <90 min) were associated with reduced in-hospital mortality. In contrast, only 2 measures (DTVI time <30min, DTP time <140 min) showed an association with increased functional independence. All measures related to acute medication and procedures, except CSC 2 (received proper endovascular recanalization), were associated with reduced in-hospital mortality and increased functional independence. Stroke unit care and dysphagia screening were associated with reduced in-hospital death and increased functional independence. In contrast, deep venous thrombosis (DVT) prophylaxis was associated with increased in-hospital mortality and decreased independence. Early rehabilitation was associated with reduced in-hospital death but decreased functional independence.

DISCUSSION

This study examined national trends for adherence to evidence-based QIs related to stroke centers in Japan from 2013 to 2017 in AIS patients receiving r-tPA and EVT using data from a nationwide quality improvement initiative, the CTGS program.[7] Furthermore, we explored the association between adherence rates and clinical outcomes. Among 25 QIs, 18 QIs showed significant ORs of adherence per year after publication of the pivotal trials in 2015, compared with 7 QIs before 2015. However, the remaining 6 QIs demonstrated no significant trends over the study period both before and after 2015. We also found an association between adherence to 14 of the 20 (25–5 QI: secondary prevention 5, IV r-tPA before EVT) QIs and reduced in-hospital death. Similarly, 11 of the 20 QIs were associated with increased functional independence at the patient level. This nationwide study demonstrated significant gaps in adherence to evidence-based QIs and association between adherence to individual evidence-based QIs and clinical outcomes of patients who received acute reperfusion therapy; it underlines the importance of nationally monitoring the quality of care by using QIs in the CTGS program.

Trends in the QI Adherence Rates Related to Stroke Centers in Japan

Our previous study enrolled the eligible cases from 2013 to 2015 and demonstrated that 5 QIs for PSCs (including DTN time <60 min) and one QI for CSCs (DTVI time <30 min) had low adherence rates.[7] This study added the cases from the second survey conducted in 2017 to demonstrate national trends in adherence per year to QIs related to stroke centers before and after the pivotal EVT for AIS trial was published.[8] Among 25 QIs, ORs of adherence by year were significant in 7 QIs before 2015 but in 18 after 2015. Using difference-in-difference analysis, we found changes of trends in adherence to QIs related to time metrics for diagnosis (eg, DTI time, DTVI time), and for EVT (eg, DTP time) and stroke education. This may be explained by increased awareness of timely EVT treatment with improved in-hospital workflow among medical professionals.[17] However, smaller OR of adherence by year to successful revascularization and NIHSS documentation after 2015 compared with that in before 2015, may reflect rapid increase of thrombectomy-capable hospitals with lower number of endovascular specialists per hospital[18] or changing indications of EVT after 2015 in a real-world situation in Japan. Further study is necessary to answer this question.

According to a 2017 systematic review,[9] the most common key performance indicators (KPIs) for stroke care quality were swallowing/nutritional assessment, stroke unit admission, antiplatelet use for ischemic stroke, brain imaging, anticoagulant use for ischemic stroke with atrial fibrillation, lipid management, DVT prophylaxis, and early physiotherapy/mobilization.

Low adherence to antiplatelet use within 48 hours of onset may be explained by the fact that ≈60% of patients had cardioembolic stroke and 80% of cases received an r-tPA infusion in this study. However, among patients who received antiplatelets within 48 hours, the proportion of atherothrombotic, cardioembolic, and lacunar stroke were 50.3, 24.5, and 10.4%, respectively. The low adherence to DVT prophylaxis may be owing to the fact that only the use of foot pumping, which has been recommended for immobilized patients

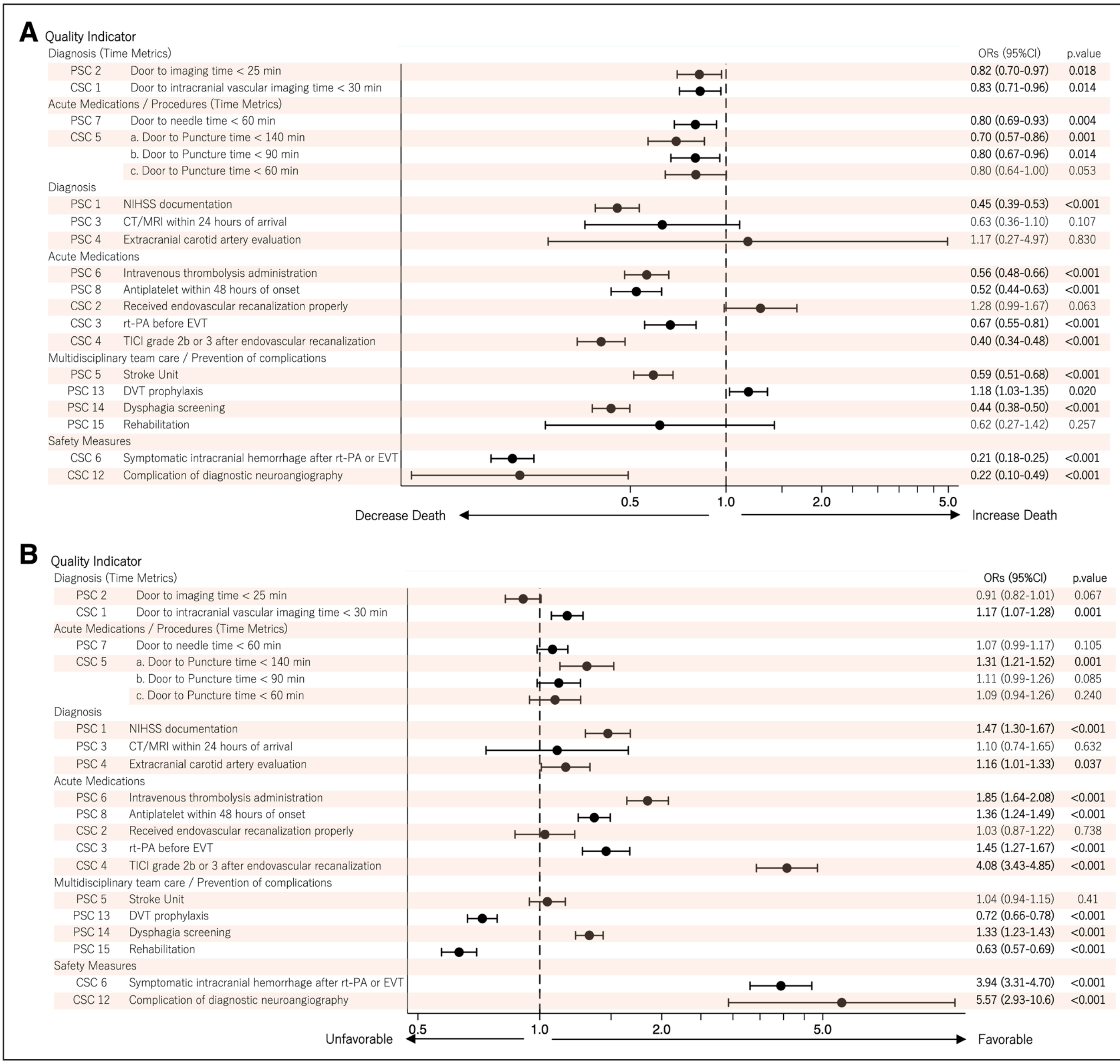

Figure 3. Associations between adherence to quality indicators and clinical outcomes.
A, Quality indicators (QIs) and in-hospital mortality. **B**, QIs and functional independence. The effect of individual adherence of QIs on clinical outcomes, using forest plots of odds ratios (ORs) for death (**A**) and a functional independence (**B**; modified Rankin Scale [mRS] score of 0–2 at discharge); Estimated OR and 95% CI of each QIs is represented by the dots and horizontal lines, respectively. ORs and 95% CIs were calculated using a mixed logistic regression model adjusted for patient characteristics, comorbidities, and hospital characteristics as a fixed effect and hospital units as a random effect. Significant differences ($P<0.05$) are indicated in bold. CSC indicates comprehensive stroke centers; CT, computed tomography; DVT, deep vein thrombosis; EVT, endovascular thrombectomy; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; r-tPA, recombinant tissue-type plasminogen activators; and TICI, Thrombolysis in Cerebral Infarction.

by the Japanese guidelines, was counted in this study. Low adherence rates of statins on discharge may be due to the relatively high prevalence of cerebral hemorrhage in Asia,[19] and a weak recommendation (grade C1) for dyslipidemia control in preventing recurrent ischemic strokes in Japanese guidelines. A recent systematic review and meta-analysis found that in patients with previous AIS, statins were associated with a significantly lower risk of recurrent AIS, mortality, and poor functional outcomes.[20]

Regarding QIs for EVT, fast reperfusion is a modifiable factor associated with better clinical outcomes when successfully performed.[21,22] A recent meta-analysis of pivotal trials showed that the intermediary outcome (ie, the rate of successful reperfusion) was higher with faster hospital arrival to groin puncture time.[22] Over the 5-year study period in this study, we observed a marked improvement in adherence to the 2 time metrics (DTN and DTP times) and one intermediary outcome (successful revascularization) after EVT. The adherence to

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these time metrics, however, remained at ≈50% in 2017. Furthermore, moderate improvement in adherence was observed in only 3 measures over the study period, suggesting the urgent need to improve the quality of stroke care in Japan.[23] The 5-year plan to conquer stroke and cardiovascular diseases in Japan, published in December 2016, encouraged the JCS training institutions to participate in the CTGS program of the J-ASPECT Study.

Associations Between Adhering to QIs Related to Stroke Centers and Clinical Outcomes

A recent systematic review found inconsistent results regarding the association between distinct evidence-based QI scores and mortality.[9] Heterogeneity of the study design, case-mix adjustments, and the length of follow-up might be one explanation for the different results. Our study demonstrates that this CTGS program can solve one of the major issues associated with using the claims databases, the lack of the NIHSS score.

Our study found an association between the adherence to 14 QIs and reduced in-hospital death. The effects in this study regarding stroke unit care, dysphagia screening, and antiplatelet use within 48 hours for patients receiving acute reperfusion therapy are comparable to those reported in a recent systematic review and meta-analysis of AIS patients.[9] In this study, the early rehabilitation adherence had a broad confidence interval and no effect on in-hospital death. In contrast, DVT prophylaxis was associated with increased in-hospital mortality rates. Measuring an association between a distinct QI and outcome has several methodological challenges that might also contribute to the heterogeneity of the previous study results.[9,10] For example, many of the defined QIs on admission might affect the results of later phase QIs, such as early dysphagia screening and the occurrence of stroke-related pneumonia. Of note, implementing DVT prophylaxis in this study was based on using foot pumping, suggesting selection bias for patients with severe stroke after acute revascularization therapy. No significant effect of early mobilization or DVT prophylaxis on in-hospital death observed in this study is consistent with the results of a recent systematic review and meta-analysis.[9]

Regarding functional outcomes at discharge, we found an association between adherence to 11 QIs and increased functional independence at discharge. A recent meta-analysis showed that reduced poor outcomes were associated with adherence to swallowing/nutritional assessment and stroke unit admission.[9]

For the length of follow-up, we examined clinical outcomes at discharge, since 61.4% of the patients at 90 days had a modified Rankin Scale score, and there was no information about postacute stroke care between discharge and 90 days. Although there has been increased global emphasis on the importance of postacute stroke care, stroke system changes have not been expanded to include postacute stroke care and follow-up, suggesting an urgent need for a paradigm shift for CSCs.[24] A recent systematic review demonstrated that the median time of scheduled follow-up for studies reporting on the association between individual KPIs and clinical outcomes was one year.[9] Thus, further effort is necessary to obtain information about postacute stroke care and recurrent stroke and modified Rankin Scale scores for longer periods.

Future Directions

Recent QI studies have implemented various components to improve care for patients with stroke or transient ischemic attack. Common elements of these multicomponent QI interventions include audit and feedback sessions and workshops.[10] A meta-analysis of QI interventions provided evidence that a combination of strategies was more effective at reducing DTN than single-intervention approaches.[25] We are now planning to assess CTGS QI adherence rate improvements over more recent years (2018–2020), after the 5-year plan to conquer stroke and cardiovascular diseases in Japan was published. Since we focused on in-hospital outcomes in this study, association between adherence to secondary prevention measures and long-term outcomes were not examined. Further study is necessary to determine whether greater adherence to secondary prevention medication improves long-term survival and quality of life after stroke.[26]

Study Limitations

Our study has several limitations. First, potential selection bias of the hospitals exists in terms of quality of stroke care. The participating hospitals are more likely to be active in quality improvement of stroke care, and hospitals with a low case volume of acute reperfusion therapies were excluded from the final dataset. Second, decreased trends in r-tPA use in the AIS patients treated with either r-tPA or EVT in this study do not mean decreased r-tPA use in total eligible AIS patients. In fact, we reported that r-tPA and EVT use increased from 4.3 to 6.4% and 0.2 to 3.0%, respectively, in AIS patients in Japan between 2010 and 2016.[13]

Third, no information regarding adherence to secondary prevention medication after discharge was available in this study. Fourth, information regarding factors, such as a living will (comfort measures only), socioeconomic status, and regular discharge, were not available in this database. The present results of DVT prophylaxis and early rehabilitation, however, were associated with decreased functional independence; the results may be explained by more common use of these measures for patients with more severe neurological deficits. Moreover, a recent meta-analysis showed that DVT prophylaxis and early rehabilitation were not significantly associated with reduced poor outcome[9]; these QIs need to be assessed with a fine change of ADL, such as the improvement of the Barthel index.

Conclusions

We provide national 5-year trends (from 2013 to 2017) in Japan regarding the adherence to evidence-based QIs related to stroke centers in patients with AIS receiving acute reperfusion therapy using the CTGS program. Marked and sustainable improvement in the adherence rates was observed for DTN time, DTP time, and successful reperfusion. We found that the adherence to individual key QIs substantially affected in-hospital outcomes. This study underlines the importance of nationally monitoring the quality of care by using QIs in the CTGS program.

ARTICLE INFORMATION

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Supplemental Material

Appendix
Tables S1–S6

REFERENCES

1. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, Ellrodt G, Cannon CP, Liang L, Peterson E, et al. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. *Circulation*. 2009;119:107–115. doi: 10.1161/CIRCULATIONAHA.108.783688
2. Smith EE, Saver JL, Alexander DN, Furie KL, Hopkins LN, Katzan IL, Mackey JS, Miller EL, Schwamm LH, Williams LS; AHA/ASA Stroke Performance Oversight Committee. Clinical performance measures for adults hospitalized with acute ischemic stroke: performance measures for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3472–3498. doi: 10.1161/STR.0000000000000045
3. Norrving B, Bray BD, Asplund K, Heuschmann P, Langhorne P, Rudd AG, Wagner M, Wiedmann S, Wolfe CD; European Implementation Score Collaboration. Cross-national key performance measures of the quality of acute stroke care in Western Europe. *Stroke*. 2015;46:2891–2895. doi: 10.1161/STROKEAHA.115.008811
4. Wiedmann S, Norrving B, Nowe T, Abilleira S, Asplund K, Dennis M, Hermanek P, Rudd A, Thijs V, Wolfe CD, et al. Variations in quality indicators of acute stroke care in 6 European countries: the European Implementation Score (EIS) Collaboration. *Stroke*. 2012;43:458–463. doi: 10.1161/STROKEAHA.111.628396
5. Iihara K, Nishimura K, Kada A, Nakagawara J, Ogasawara K, Ono J, Shiokawa Y, Aruga T, Miyachi S, Nagata I, et al. Effects of comprehensive stroke care capabilities on in-hospital mortality of patients with ischemic and hemorrhagic stroke: J-ASPECT study. *PLoS One*. 2014;9:e96819. doi: 10.1371/journal.pone.0096819
6. Nishimura A, Nishimura K, Onozuka D, Matsuo R, Kada K, Kamitani S, Higashi T, Ogasawara K, Shimodozono M, Harada M, et al. Development of quality indicators of stroke centers and feasibility of their measurement using a nationwide insurance claims database in Japan J-ASPECT Study. *Circ J*. 2019;83:2292–2302. doi: 10.1253/circj.CJ-19-0089
7. Ren N, Nishimura A, Kurogi A, Nishimura K, Matsuo R, Ogasawara K, Hashimoto Y, Higashi T, Sakai N, Toyoda K, et al. Measuring quality of care for ischemic stroke treated with acute reperfusion therapy in Japan —. *Circ J*. 2021;85:201–209. doi: 10.1253/circj.CJ-20-0639
8. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, et al; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
9. Urimubenshi G, Langhorne P, Cadilhac DA, Kagwiza JN, Wu O. Association between patient outcomes and key performance indicators of stroke care quality: a systematic review and meta-analysis. *Eur Stroke J*. 2017;2:287–307. doi: 10.1177/2396987317735426
10. Kilkenny MF, Bravata DM. Quality improvement. *Stroke*. 2021;52:1866–1870. doi: 10.1161/STROKEAHA.121.033451
11. Man S, Zhao X, Uchino K, Hussain MS, Smith EE, Bhatt DL, Xian Y, Schwamm LH, Shah S, Khan Y, et al. Comparison of acute ischemic stroke care and outcomes between comprehensive stroke centers and primary stroke centers in the United States. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004512. doi: 10.1161/CIRCOUTCOMES.117.004512
12. Haas K, Rücker V, Hermanek P, Misselwitz B, Berger K, Seidel G, Janssen A, Rode S, Burmeister C, Matthis C, et al; German Stroke Register Study Group (ADSR). Association between adherence to quality indicators and 7-day in-hospital mortality after acute ischemic stroke. *Stroke*. 2020;51:3664–3672. doi: 10.1161/STROKEAHA.120.029968
13. Kada A, Ogasawara K, Kitazono T, Nishimura K, Sakai N, Onozuka D, Shiokawa Y, Miyachi S, Nagata I, Toyoda K, et al. National trends in outcomes of ischemic stroke and prognostic influence of stroke center capability in Japan, 2010–2016. *Int J Stroke*. 2019;1747493019884526. doi: 10.1177/1747493019884526
14. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM; RECORD Working Committee. The reporting of studies conducted using observational routinely-collected health data (RECORD) statement. *PLoS Med*. 2015;12:e1001885. doi: 10.1371/journal.pmed.1001885
15. Sacks D, Baxter B, Campbell BCV, Carpenter JS, Cognard C, Dippel D, Eesa M, Fischer U, Hausegger K, Hirsch JA, et al. Multisociety consensus quality improvement revised consensus statement for endovascular therapy of acute ischemic stroke. *Int J Stroke*. 2018;13:612–632. doi: 10.1177/1747493018778713
16. McTaggart RA, Ansari SA, Goyal M, Abruzzo TA, Albani B, Arthur AJ, Alexander MJ, Albuquerque FC, Baxter B, Bulsara KR, et al; Standards and Guidelines Committee of the Society of NeuroInterventional Surgery (SNIS). Initial hospital management of patients with emergent large vessel occlusion (ELVO): report of the standards and guidelines committee of the

Society of NeuroInterventional Surgery. *J Neurointerv Surg*. 2017;9:316–323. doi: 10.1136/neurintsurg-2015-011984

17. Wang Y, Li Z, Zhao X, Liu L, Wang C, Peterson ED, Schwamm LH, Fonarow GC, Smith SC, et al. Evidence-based performance measures and outcomes in patients with acute ischemic stroke findings from the China National Stroke Registry. *Circ Cardiovasc Qual Outcomes*. 2018;11:e001968. doi: 10.1161/CIRCOUTCOMES.115.001968
18. Kurogi A, Onozuka D, Hagihara A, Nishimura K, Kada A, Hasegawa M, Higashi T, Kitazono T, Ohta T, Sakai N, et al; J-ASPECT Study Collaborators. Influence of hospital capabilities and prehospital time on outcomes of thrombectomy for stroke in Japan from 2013 to 2016. *Sci Rep*. 2022;12:3252. doi: 10.1038/s41598-022-06074-1
19. Ueshima H, Sekikawa A, Miura K, Turin TC, Takashima N, Kita Y, Watanabe M, Kadota A, Okuda N, Kadowaki T, et al. Cardiovascular disease and risk factors in Asia: a selected review. *Circulation*. 2008;118:2702–2709. doi: 10.1161/CIRCULATIONAHA.108.790048
20. Ziff OJ, Banerjee G, Ambler G, Werring DJ. Statins and the risk of intracerebral haemorrhage in patients with stroke: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2019;90:75–83. doi: 10.1136/jnnp-2018-318483
21. Janssen PM, Venema E, Dippel DWJ. Effect of workflow improvements in endovascular stroke treatment. *Stroke*. 2019;50:665–674. doi: 10.1161/STROKEAHA.118.021633
22. Bourcier R, Goyal M, Liebeskind DS, Muir KW, Desal H, Siddiqui AH, Dippel DWJ, Majoie CB, van Zwam WH, Jovin TG, et al; HERMES Trialists Collaboration. Association of time from stroke onset to groin puncture with quality of reperfusion after mechanical thrombectomy: a meta-analysis of individual patient data from 7 randomized clinical trials. *JAMA Neurol*. 2019;76:405–411. doi: 10.1001/jamaneurol.2018.4510
23. Wells S, Tamir O, Gray J, Naidoo D, Bekhit M, Goldmann D. Are quality improvement collaboratives effective? A systematic review. *BMJ Qual Saf*. 2018;27:226–240. doi: 10.1136/bmjqs-2017-006926
24. Duncan PW, Bushnell C, Sissine M, Coleman S, Lutz BJ, Johnson AM, Radman M, Pvru Bettger J, Zorowitz RD, Stein J. Comprehensive stroke care and outcomes: time for a paradigm shift. *Stroke*. 2021;52:385–393. doi: 10.1161/STROKEAHA.120.029678
25. Siarkowski M, Lin K, Li SS, Al Sultan A, Ganshorn H, Kamal N, Hill M, Lang E. Meta-analysis of interventions to reduce door to needle times in acute ischaemic stroke patients. *BMJ Open Qual*. 2020;9:e000915. doi: 10.1136/bmjoq-2020-000915
26. Kilkenny MF, Phan HT, Lindley RI, Kim J, Lopez D, Dalli LL, Grimley R, Sundararajan V, Thrift AG, Andrew NE, et al; Stroke123 Investigators and the AuSCR Consortium. Utility of the hospital frailty risk score derived from administrative data and the association with stroke outcomes. *Stroke*. 2021;52:2874–2881. doi: 10.1161/STROKEAHA.120.033648