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Effect of a Multifaceted Quality Improvement Intervention on Hospital Personnel Adherence to Performance Measures in Patients With Acute Ischemic Stroke in China
A Randomized Clinical Trial

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IMPORTANCE In China and other parts of the world, hospital personnel adherence to evidence-based stroke care is limited.

OBJECTIVE To determine whether a multifaceted quality improvement intervention can improve hospital personnel adherence to evidence-based performance measures in patients with acute ischemic stroke (AIS) in China.

DESIGN, SETTING, AND PARTICIPANTS A multicenter, cluster-randomized clinical trial among 40 public hospitals in China that enrolled 4800 patients hospitalized with AIS from August 10, 2014, through June 20, 2015, with 12-month follow-up through July 30, 2016.

INTERVENTIONS Twenty hospitals received a multifaceted quality improvement intervention (intervention group; 2400 patients), including a clinical pathway, care protocols, quality coordinator oversight, and performance measure monitoring and feedback. Twenty hospitals participated in the stroke registry with usual care (control group; 2400 patients).

MAIN OUTCOMES AND MEASURES The primary outcome was hospital personnel adherence to 9 AIS performance measures, with co-primary outcomes of a composite of percentage of performance measures adhered to, and as all-or-none. Secondary outcomes included in-hospital mortality and long-term outcomes (a new vascular event, disability [modified Rankin Scale score, 3-5], and all-cause mortality) at 3, 6, and 12 months.

RESULTS Among 4800 patients with AIS enrolled from 40 hospitals and randomized (mean age, 65 years; women, 1757 [36.6%]), 3980 patients (82.9%) completed the 12-month follow-up of the trial. Patients in intervention group were more likely to receive performance measures than those in the control groups (composite measure, 88.2% vs 84.8%, respectively; absolute difference, 3.54% [95% CI, 0.68% to 6.40%], $P = .02$). The all-or-none measure did not significantly differ between the intervention and control groups (53.8% vs 47.8%, respectively; absolute difference, 6.69% [95% CI, −0.41% to 13.79%], $P = .06$). New clinical vascular events were significantly reduced in the intervention group compared with the control group at 3 months (3.9% vs 5.3%, respectively; difference, −2.03% [95% CI, −3.51% to −0.55%]; $P = .007$), 6 months (6.3% vs 7.8%, respectively; difference, −2.18% [95% CI, −4.0% to −0.35%]; $P = .02$) and 12 months (9.1% vs 11.8%, respectively; difference, −3.13% [95% CI, −5.28% to −0.97%]; $P = .005$).

CONCLUSIONS AND RELEVANCE Among 40 hospitals in China, a multifaceted quality improvement intervention compared with usual care resulted in a statistically significant but small improvement in hospital personnel adherence to evidence-based performance measures in patients with acute ischemic stroke when assessed as a composite measure, but not as an all-or-none measure. Further research is needed to understand the generalizability of these findings.

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The overall global burden of stroke has increased in the past several decades in developing countries.[1] Stroke is the leading cause of death and adult disability in China,[2] with an estimated 2.4 million new stroke events in 2013.[3] Large-scale randomized trials and systematic reviews have established the efficacy of several performance measures for acute ischemic stroke, such as intravenous recombinant tissue plasminogen activator (rtPA or alteplase), antiplatelet therapy, and anticoagulation for patients with atrial fibrillation.[4,5] However, adherence to these evidence-based performance measures is suboptimal and gaps in adherence to guideline-recommended care are even greater in China.[6]

Multifaceted quality improvement interventions that address the barriers to care are effective in changing physician practices.[7-9] Quality improvement interventions have demonstrated that stroke care quality can be improved by conducting interventions such as using clinical pathways, training physicians on evidence-based guidelines, auditing care delivery, and providing timely feedback.[10,11] Nevertheless, previous cluster-randomized studies in this area have had conflicting results. Some studies have demonstrated significant improvements in health care quality from quality improvement interventions,[12,13] whereas others have found no significant effect.[14,15] However, to our knowledge, randomized clinical trials have not been used to assess the effectiveness of multifaceted quality improvement interventions of stroke care in developing countries, which have up to 78% of the global burden of stroke.[1] Furthermore, the effect of these process improvement interventions on short-term or long-term clinical outcomes needs to be explored further.

Therefore, a cluster-randomized clinical trial called Intervention to Bridge the Evidence-based Gap in Stroke Care Quality (GOLDEN BRIDGE–AIS) was conducted to examine the effectiveness of a multifaceted quality improvement intervention on hospital personnel adherence to evidence-based performance measures and outcomes in patients with acute ischemic stroke (AIS) in China.

Key Points

Question Can a multifaceted quality improvement intervention increase hospital personnel adherence to 9 evidence-based performance measures in patients with acute ischemic stroke in China?

Findings In this cluster-randomized clinical trial that included 4800 patients from 40 hospitals, hospital personnel in the intervention group adhered to 88.2% of the evidence-based performance measures and those in the control group adhered to 84.8% of the performance measures, a difference that was statistically significant. However, for the co-primary outcome of adherence to all 9 performance measures, there was no significant difference.

Meaning A multifaceted intervention, compared with usual care, resulted in a small improvement in personnel adherence to evidence-based performance measures when assessed as a composite measure but not as an all-or-none measure.

Methods

Study Design

Details of this trial's design and methods have been published elsewhere and in Supplement 1.[16] Briefly, this trial was an open-label, cluster-randomized clinical trial. The main aims were to evaluate the effect of a multifaceted quality improvement intervention on adherence to evidence-based performance measures for patients with AIS during the acute phase of care and at discharge and patient outcomes such as new vascular events, disability, and mortality at 3, 6, and 12 months after stroke onset. The trial protocol was approved by the central institutional review board at Beijing Tiantan Hospital. In addition, all participating clusters received the approval by their local research ethics board. Written consent was obtained at the cluster (hospital)-level from the hospital medical director. Consent was also obtained from patients or their proxy for participation in a telephone survey at 3, 6, and 12 months after the initial stroke. The formal patient enrollment period was from August 10, 2014, through June 20, 2015, with follow-up through July 30, 2016.

Hospitals

Hospitals were enrolled from the China National Network of Stroke Research (now the Chinese Stroke Center Alliance). The Chinese Stroke Center Alliance, established by the National Center of Quality Management in Neurological Diseases Care (formerly the National Center of Quality Management in Stroke Care), includes 563 hospitals from 27 provinces and 4 municipalities (total 31 locations) in Mainland China. In China, hospitals are classified into 3 grades: community hospitals are defined as primary grade, hospitals that serve several communities are defined as secondary grade, and central hospitals for a certain district or city are defined as tertiary grade.[17] Hospital regions are divided into eastern, central, and western areas according to the annual report on health statistics of China.[18] Only secondary or tertiary public hospitals with emergency departments (EDs) and neurological wards that admit patients with stroke and had the capacity to administer intravenous rtPA were eligible to participate in this trial. Primary hospitals, private hospitals, and hospitals in rural regions were excluded.

Patients

At participating hospitals, we consecutively enrolled eligible patients with AIS according to the standardized definition.[5,19] Patients 18 years or older with AIS confirmed by brain computed tomography scan or magnetic resonance imaging within 7 days after symptom onset and admitted to wards directly or through the ED were included. Patients with other cerebrovascular disease, such as hemorrhagic stroke, transient ischemic attack, cerebral venous sinus thrombosis, or noncerebrovascular diseases, were excluded.

Baseline Survey

We conducted a survey among all participating hospitals to obtain the baseline adherence to the evidence-based performance measures, ensure comparability between intervention

and control groups at each hospital, and obtain a reliable estimation of the sample size. Methods and results of this baseline survey were presented in eAppendix A in Supplement 2.

Cluster Randomization and Blinding

Forty eligible hospitals were randomly selected and stratified by the following characteristics: province, hospital capacity (secondary grade or tertiary), and baseline level of stroke care quality. This was done by an independent statistician not otherwise involved in the study. These clusters were randomized 1:1 to a multifaceted quality improvement intervention (intervention group) or routine care plus stroke registry participation (control group) by using a randomly generated number (SAS [SAS Institute], version 9.3 software). Given the nature of the multifaceted intervention, only the independent outcome evaluators and statisticians were blinded to the intervention.

Stroke Quality Improvement Interventions

The multifaceted quality improvement intervention included an evidence-based clinical pathway, written care protocols for implementation of performance measures, a full-time quality coordinator, and a monitoring and feedback system for performance measures. Two physicians from each of the intervention clusters (the director of the department of neurology acting as a local investigator and a physician or nurse acting as a quality coordinator) attended a 2-day workshop designed to educate the hospital personnel on this trial about quality improvement intervention. These 2 trained professionals took charge of sharing these operational methods with cluster personnel who took care of patients with stroke.

The evidence-based clinical pathway was written by a panel of stroke experts according to the published statements in peer-reviewed literature, consensus statements and guidelines.[5,19] It was integrated into the care plan of each eligible stroke admission. This pathway consisted of general guideline-based recommendations for acute stroke management, and a specific daily care plan for each of the first 7 days of the acute admission and discharge.

Written care protocols for the implementation of performance measures were provided for all intervention clusters, and included the following: intravenous rtPA protocol; a deep venous thrombosis (DVT) prophylaxis protocol; a swallowing dysfunction management protocol; evidence-based medications protocols for antithrombotic therapy after admission and at discharge; anticoagulation for patients with atrial fibrillation; guidelines for prescribing statin medications; and guidelines for prescribing antihypertensive and hypoglycemic medications when appropriate.

A trained physician or nurse in each intervention cluster acted as a quality coordinator. The responsibility of the quality coordinator included interacting with physicians once gaps in the application of evidence-based interventions were identified, ensuring that all components of the quality improvement intervention were implemented for patients with AIS, identifying barriers to the implementation, and training the health care staff involved with the care of the patients.

A monitoring and feedback system, as well as a cyclical model of predefined performance measures, was designed to automatically analyze and provide feedback to the team providing quality stroke care in the intervention group. An independent quality management account was assigned to the quality coordinator of all of the intervention clusters to log in to the monitoring and feedback system. The intervention cluster's investigators or quality coordinator were required to check their level of adherence to the predefined performance measures at least once a week and compare the observed performance with performance measured to-date and performance by other clusters.

Data Collection

In all participating clusters, data were obtained prospectively and entered into a web-based data entry system by a local, trained independent research coordinator who was not involved in the care of patients and received compensation from this trial. Range checks were used to check for inconsistent or out-of-range data and prompted the user to correct or review data entries outside the predefined range. The system also provided predefined logic checks to identify errors or illogical data entries. A data quality meeting was held monthly to review all the hospital enrollment records and registry data.

Outcomes

The primary outcomes were adherence to the 9 predefined evidence-based performance measures in patients with AIS, 6 of which were designed to be the same as the Get With The Guidelines-Stroke (GWTG-Stroke) performance measures.[10] These included 4 performance measures at the beginning of hospitalization (intravenous rtPA treatment within 3 hours of symptom onset, early use of antithrombotics, dysphagia screening, and DVT prophylaxis) and 5 performance measures at discharge (use of antithrombotics, anticoagulation for patients with atrial fibrillation or flutter, use of a lipid-lowering agent for low-density lipoprotein [LDL] of more than 100 mg/dL or undocumented LDL [to convert to mmol/L, multiply by 0.0259], use of antihypertension medication, and treatment of diabetes). Detailed performance measure specifications and contraindications are shown in eTable 1 in Supplement 2.

Adherence was expressed as an all-or-none measure or a composite measure as co-primary outcomes if either one was statistically significant, the study was to be interpreted as "positive." The all-or-none measure was defined as the proportion of patients who received all of the performance measures for which the patient was eligible. The composite measure was defined as the total number of eligible performance measures performed divided by the total number of performance measures for which a given patient was eligible. The composite measure was calculated for each patient and then averaged.[10]

The secondary outcomes included in-hospital death, a new clinical vascular event (ischemic stroke, hemorrhagic stroke, myocardial infarction, or vascular death), disability as measured by modified Rankin Scale (mRS; score of 3-5); and all-cause mortality at 3, 6, and 12 months after initial symptom onset. Trained research personnel were blinded to the intervention and used standardized scripts to contact patients or

caregivers by telephone at 3, 6, and 12 months.[16] Symptomatic intracerebral hemorrhage was recorded in patients treated with intravenous rtPA. Symptomatic intracerebral hemorrhage was defined as any type of intracerebral hemorrhage on any posttreatment imaging related to any worsening in neurological condition.[20]

Sample Size

A prerandomization survey at participating clusters was conducted. The mean composite score of stroke care quality was 80%. According to the GWTG-Stroke program, the guideline adherence to individual performance measures was increased 4.33% from baseline (83.52%) to the first year after the implementation (87.85%) of GWTG-Stroke.[10] Therefore, a total of 4800 patients at 40 hospitals (considering a median of 120 patients with AIS per hospital) would be required to detect a 5% improvement in the composite evidence-based performance measures in patients with AIS, with 80% power, 5% significance level, and an intracluster correlation coefficient (ICC) of 0.02.[10] According to this predefined sample size, each group was required to enroll 2400 patients. The web-based patient management tool was used to enter patient's data and monitor the enrollment number of patients. When 2400 eligible patients were recruited for a group, the enrollment for that group was stopped.

Data Analysis

We used intention-to-treat analysis for all outcomes.[21] The baseline characteristics of hospitals and patients were analyzed to assess cluster differences between intervention and control groups. We summarized continuous variables as median with interquartile ranges and categorical variables as frequency and percentage. We analyzed continuous and categorical data by using Wilcoxon rank-sum test and χ^2 test separately.[16] With all comparative outcomes, cumulative incidences and absolute differences with 95% CIs were presented and adjusted by patient and hospital baseline characteristics.

Modes were used to impute missing values of categorical variables, and medians were imputed for missing values of continuous variables. Smoking status had the highest proportion of missing values at 1.42%, which were replaced with the value of no smoking history. Only one patient had a missing National Institutes of Health Stroke Scale (NIHSS) score, which was replaced by the median value of 3.

Multivariable regression models were performed to compare the outcomes between intervention and control groups. Generalized estimating equations were used to account for within-hospital correlation. Logistic regression was performed for the binary all-or-none measure and disability outcomes. The composite measure was expressed as the odds of fulfilling care opportunities for which a patient was eligible. Thus in the analysis of the composite measure, each care opportunity contributed an observation in the analysis, and the outcome was a dichotomized (1 = measure met vs 0 = measure not met).[6,10] For example, if a particular patient was eligible for 5 of the 7 performance measures and only received 3 of them, this patient contributed 5 observations to the analysis; 3 of the measures would have an outcome value of 1 and 2 would have an outcome value of 0. The effects of intervention were expressed as a population average odds ratio (OR_{PA}).[9] The clinical vascular events and mortality at discharge and at 3, 6, and 12 months after initial symptom onset were analyzed as time-to-event outcomes. A mixed-model with a binary link function was used for 3-, 6-, and 12-month disability. These outcomes were demonstrated by Kaplan-Meier curves and assessed by using multivariable Cox proportional hazards models. To assess that the improvement in performance measure compliance in the intervention group was not due to the increased documentation of contraindications (smaller denominator not larger numerator), a sensitivity analysis that included patients with contraindications for evidence-based interventions in the denominator of the overall population was conducted. All multivariable models adjusted for patient characteristics (including age, sex, history of ischemic stroke, hypertension disease, diabetes, hyperlipidemia, atrial fibrillation, coronary artery disease and previous myocardial infarction, ever smoking, and NIHSS score at admission) and hospital characteristics (including hospital capacity [tertiary and secondary], region, stroke unit, teaching hospital status, and number of neurological ward beds). There was no adjustment multiple comparison for co-primary outcome measures. All secondary analyses were interpreted to be exploratory. A *P* value less than .05 was considered statistically significant; all tests were 2-sided. All statistical analyses were performed by using SAS (SAS Institute), version 9.3.

Results

A total of 40 hospitals from 18 provinces were initially recruited into the trial. Three hospitals, which had unexpected inability to conduct this trial, were replaced according to their characteristics. Finally, 40 hospitals were included. A total of 4800 patients were enrolled prospectively and included in the primary analysis (**Figure 1**). None of the clusters were further excluded from this trial. The duration of enrolling patients was 207 days (interquartile range [IQR], 182-225) in the intervention group and 204 days (IQR, 159-262) in the control group.

Table 1 shows the characteristics of patients and hospitals in the baseline survey and intervention and control groups. The mean age of the patients enrolled was 65 years and 36.6% were women. From these participating hospitals, 72.5% were tertiary hospitals, 62.5% had a stroke unit, 62.5% were teaching hospitals, and the median annual number of beds of neurological wards was 77 (IQR, 61-178). The mean number of patients in each cluster was 120 (range, 102-145). Patient and hospital characteristics were balanced between intervention and control groups except for length of stay. There were 2003 patients (83.5%) in the intervention group and 1977 patients (82.4%) in the control group who completed 12-month follow-up. Baseline characteristics of patients with and without the 1-year mRS measurement are shown in eTable 2 in Supplement 2.

Adherence to Evidence-Based Performance Measures

In the intervention group, the median time interval between monitoring of the AIS performance measures and subsequent

feedback was 7 days. Adherence to evidence-based performance measures is summarized in **Table 2**. Patients in the intervention group were more likely to receive eligible performance measures (composite measure) than those in the control group after adjusting for patient and hospital baseline characteristics (88.2% in the intervention group vs 84.8% in the control group; absolute difference, 3.54% [95% CI, 0.68% to 6.40%], P = .02; adjusted OR_{PA}, 1.39 [95% CI, 1.12 to 1.72]; ICC, 0.02; P = .003). The all-or-none measure was numerically higher in the intervention group (53.8%) than in the control group (47.8%), but this did not reach statistical significance (absolute difference, 6.69% [95% CI, −0.41% to 13.79%], P = .06; adjusted OR_{PA}, 1.19 [95% CI, 0.85 to 1.67]; ICC, 0.07; P = .31) (Table 2). Although the adherence to each of the 9 performance measures was higher in intervention hospitals than that in control hospitals, there were no statistically significant differences at the individual measure level except for 2 performance measures: DVT prophylaxis and antidiabetic medication.

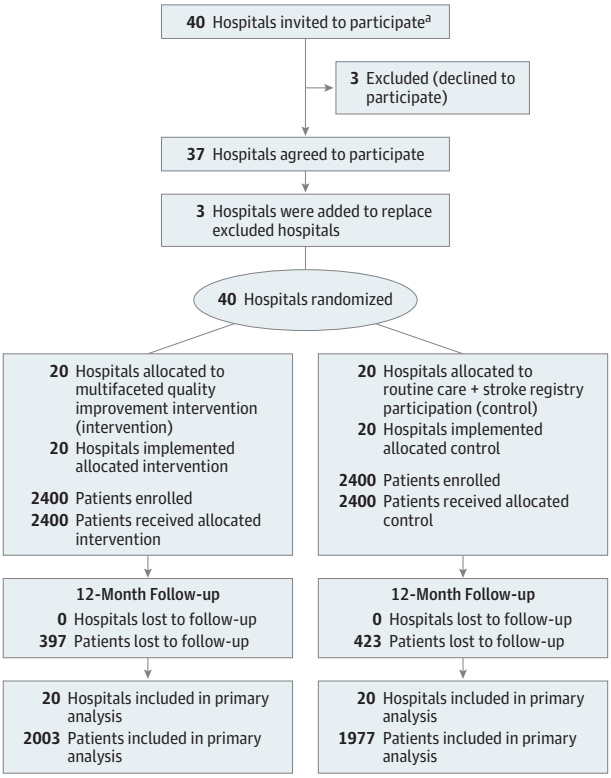
Clinical Events

Table 3 shows in-hospital and long-term mortality, the new clinical vascular events, and disability outcomes at 3, 6, and 12 months after discharge. New clinical vascular events (ischemic stroke, hemorrhagic stroke, myocardial infarction, or vascular death, shown in the eTable 3 in Supplement 2, respectively) were lower in the intervention group than the control group for each time point (intervention group vs control group: 3 months, 3.9% vs 5.3% [absolute difference, −2.03% {95% CI, −3.51% to −0.55%}, hazard ratio {HR}, 0.65 {95% CI, 0.49 to 0.86}]; 6 months, 6.3% vs 7.8% [absolute difference, −2.18% {95% CI, −4.0% to −0.35%}, HR, 0.72 {95% CI, 0.57 to 0.90}]; and 12 months, 9.1% vs 11.8% [absolute difference, −3.13% {95% CI, −5.28% to −0.97%}, HR, 0.72 {95% CI, 0.60 to 0.87}]) (Table 3 and **Figure 2**A). Stroke disability was also lower in the intervention group than the control group for each time point (intervention group vs control group: 3 months, 19.2% vs 21.0% [absolute difference, −3.72% {95% CI, −6.7% to −0.79%}, odds ratio {OR}, 0.76 {95% CI, 0.63 to 0.91}]; 6 months, 15.8% vs 17.9% [absolute difference, −3.86% {95% CI, −6.60% to −1.13%}, OR, 0.74 {95% CI, 0.61 to 0.89}]; and 12 months, 12.7% vs 14.7% [absolute difference, −3.13% {95% CI, −5.80% to −0.46%}, OR, 0.74 {95% CI, 0.59 to 0.93}]). There was no significant difference in total mortality rates in the hospital and at 3, 6, and 12 months (Figure 2B). Symptomatic intracerebral hemorrhage in patients receiving intravenous rtPA did not differ significantly between the intervention and control groups (2.2% [1 of 46 patients] in the intervention group vs 8.7% [2 of 23 patients] in the control group, P = .26).

Sensitivity Analysis

A sensitivity analysis, which included patients with contraindications for evidence-based interventions in the denominator of the overall population, was conducted. The composite measure remained higher in the quality improvement intervention group than the control group (85.3% in the intervention group vs 80.91% in the control group [absolute difference, 4.20% {95% CI, 1.77% to 6.63%}, adjusted OR_{PA}, 1.36 {95% CI, 1.11 to 1.67}; P = .003]), shown in eTable 4 in Supplement 2.

Figure 1. Flow of Hospitals and Patients Through the Study



[a] Forty eligible hospitals were selected randomly and invited from 563 hospitals of the China National Network of Stroke Research according to hospital grade (tertiary and secondary) and region (eastern, central, and western).

Discussion

In this cluster-randomized clinical trial, a multifaceted quality improvement intervention was effective in improving the quality of acute stroke care in public hospitals in China. These quality improvement interventions significantly improved short-term and long-term outcome in reductions of new vascular events and reduced stroke disability.

This study focused on improving the quality of care for patients admitted to public hospitals in China who have fewer resources and lower personal income than patients represented in prior studies from Western Europe and the United States.[12,13] Public hospitals are the main source of physicians, accounting for 92% of hospital admissions in China.[22] These public hospitals are overcrowded with patients and have limited resources. These findings suggest that despite these limitations, quality improvement interventions are feasible and could still be successful. Furthermore, these interventions are simple and do not require expensive technology or complex medical intervention. However, except for DVT prophylaxis and

Table 1. Baseline Characteristics of Hospitals and Patients With Acute Ischemic Stroke Implementing Multifaceted Quality Improvement Intervention (Intervention) vs Routine Care + Stroke Registry Participation Group (Control) in China

	Baseline Survey, No. (%)	Intervention Group, No. (%)	Control Group, No. (%)
Hospital Characteristics			
Hospitals, No.	40	20	20
Hospital grade			
Tertiary	29 (72.5)	15 (75.0)	14 (70.0)
Secondary	11 (27.5)	5 (25.0)	6 (30.0)
Region			
Eastern	20 (50)	10 (50.0)	10 (50.0)
Central	9 (22.5)	4 (20.0)	5 (25.0)
Western	11 (27.5)	6 (30.0)	5 (25.0)
Stroke unit	25 (62.5)	14 (70.0)	11(55.0)
Teaching hospital	25 (62.5)	13 (65.0)	12(60.0)
No. of neurological ward beds, median (IQR)	77 (61-178)	70 (60-138)	80 (61-152)
Annual stroke discharges, median (IQR)	401 (321-761)	365 (317-710)	417 (321-785)
Patient Characteristics			
Patients, No.	801	2400	2400
Demographics			
Age, median (IQR), y	65 (57-75)	65 (57-73)	64 (56-74)
Men	486 (60.7)	1553 (64.7)	1490 (62.1)
Medical history			
Ischemic stroke	271 (33.8)	666 (27.8)	722 (30.1)
Diabetes	193 (24.1)	577 (24.0)	509 (21.2)
Hypertension	542 (67.7)	1550 (64.6)	1540 (64.2)
Dyslipidemia	65 (8.1)	305 (12.7)	291 (12.1)
CAD/previous myocardial infarction	126 (15.7)	311 (13.05)	298 (12.4)
Atrial fibrillation	67 (8.4)	118 (4.9)	127 (5.3)
Ever smoking	339 (42.3)	1057 (44.0)	1059 (44.1)
NIHSS score at admission, median (IQR)	4 (2-8)	4 (2-6)	4 (2-6)
Transported to ED by EMS	112 (14.0)	265 (11.0)	236 (9.9)
Proportion of patients with time from symptom onset to ED arrival within 2 h, %	96 (12.0)	254 (10.6)	238 (9.9)
LDL, median (IQR), mg/dL	111.97 (88.80-135.14)	103.08 (81.85-126.25)	103.86 (80.69-128.57)
Length of stay, median (IQR), d	13 (10-15)	13 (10-15)	12 (9.5-15)

Abbreviations: CAD, coronary artery disease; ED, emergency department; EMS, emergency medical service; IQR, interquartile range; LDL, low-density lipoprotein; NIHSS, National Institutes of Health Stroke Scale (range, 0-42 [most severe]).

SI conversion factor: To convert LDL to mmol/L, multiply by 0.0259.

antidiabetic medication at discharge, the differences at the level of each individual performance measure between the 2 groups did not reach significance. These findings do not imply that the multifaceted intervention tools only worked on these 2 performance measures: DVT prophylaxis and antidiabetic medication at discharge. The performance on the all-or-none measure was not better in the hospitals receiving quality improvement intervention in this trial. In the all-or-none measure, no credit is given for patients who receive some, but not all, required performance measures.[23] Longer-lasting interventions might be needed to identify a significant difference in the all-or-none measure.

This study identified that this multifaceted quality improvement intervention was effective and workable in clinical settings in China to increase hospital personnel adherence to evidence-based performance measures of stroke care and decrease the short-term and long-term rates of new vascular events and disability among patients with AIS. A part of these findings is consistent with those of large, stroke care quality improvement registries, such as American Heart Association/American Stroke Association's GWTG-Stroke.[10,11] The GWTG-Stroke program worked with participating hospitals and implemented these guidelines by providing quality improvement consultation, workshops, and webinars. GWTG-Stroke is also supported by a web-based patient management tool not only for data collection, but also for providing decision support and real-time online reporting.[11] Significant improvements in the quality of care were observed from 2003 to 2009 with a composite measure improvement from 83.52% to 93.97%.[24] In the national quality improvement initiative Target: Stroke, which employed 10 key evidence-based strategies, the results were convincing: improved timeliness of intravenous rtPA administration following AIS on a national scale with associated improvements in clinical outcomes.[25] However, both GWTG-Stroke and Target: Stroke projects were not randomized clinical trials, which may lead to overestimation of

Table 2. Adherence to Evidence-Based Performance Measures Among Eligible Patients With Acute Ischemic Stroke Receiving a Multifaceted Quality Improvement Intervention (Intervention) vs Routine Care + Stroke Registry Participation Group (Control) in China

	Intervention Group, No. of Events/Total Patients (%)	Control Group, No. of Events/Total Patients (%)	Absolute Difference (95% CI), %[a]	*P* Value	Population Average Odds Ratio (95% CI)[a]	*P* Value	Intracluster Correlation Coefficient
Composite measure, mean (SD)	88.2 (15.1)	84.8 (18.2)	3.5 (0.7-6.4)	.02	1.39 (1.12-1.72)	.003	0.02
All-or-none measure	1290/2400 (53.8)	1147/2400 (47.8)	6.7 (−0.4 to 13.8)	.06	1.19 (0.85 to 1.67)	.31	0.07
Performance measures at the beginning of hospitalization							
Intravenous rtPA within 3 hours of symptom onset[b]	46/212 (21.7)	23/204 (11.3)	7.3 (−5.3 to 19.9)	.26	3.18 (0.94 to 10.78)	.06	0.28
Early antithrombotics[c]	2307/2353 (98.0)	2253/2330 (96.7)	1.5 (−0.3 to 3.2)	.10	1.93 (0.94 to 3.95)	.07	0.03
Dysphagia screening[d]	2255/2328 (96.9)	2040/2139 (95.4)	1.6 (−2.1 to 5.3)	.41	2.49 (0.84 to 7.40)	.10	0.24
DVT prophylaxis[e]	178/645 (27.6)	66/592 (11.1)	15.6 (3.3 to 27.9)	.01	2.42 (1.02 to 5.72)	.04	0.36
Performance measures at discharge							
Antithrombotics[f]	2272/2324 (97.8)	2141/2305 (92.9)	4.2 (−0.6 to 8.9)	.09	2.29 (0.86 to 6.11)	.10	0.23
Anticoagulation for atrial fibrillation	63/155 (40.6)	39/137 (28.5)	12.9 (−5.8 to 31.6)	.18	1.80 (0.68 to 4.75)	.23	0.25
Lipid-lowering for LDL >100 mg/dL	1415/1481 (95.5)	1439/1547 (93.0)	2.4 (−1.6 to 6.4)	.25	1.35 (0.67 to 2.73)	.40	0.16
Antihypertensive medication	1510/1838 (82.2)	1372/1771 (77.5)	6.1 (−0.6 to 12.7)	.07	1.44 (0.94 to 2.20)	.10	0.08
Antidiabetic medication	653/728 (89.7)	557/663 (84.0)	5.0 (0.8 to 9.3)	.02	1.57 (1.08 to 2.28)	.02	0.03

Abbreviations: DVT, deep vein thrombosis; LDL, low-density lipoprotein; rtPA, recombinant tissue plasminogen activator (alteplase).

SI conversion factor: To convert LDL to mmol/L, multiply by 0.0259.

[a] Positive values favor the intervention group. Adjusted for patient and hospital characteristics, including age, sex, history of ischemic stroke, hypertension disease, diabetes, hyperlipidemia, atrial fibrillation, coronary artery disease and previous myocardial infarction, ever smoking, National Institutes of Health Stroke Scale score at admission, hospital grade, region, stroke unit, teaching hospital status, and No. of neurological ward beds.

[b] Patients who arrived within 2 h after initial symptom onset and were treated within 3 h of symptom onset.

[c] Antithrombotic therapy prescribed within 48 h of hospitalization.

[d] Conducted prior to any oral intake during hospitalization.

[e] Conducted among patients (nonambulatory) by end of hospital day 2.

[f] Aspirin, clopidogrel, ozagrel, dipyridamole, ticlopidine, cilostazol, low-molecular-weight heparin, unfractionated heparin, and warfarin.

the effect of the intervention. A cluster-randomized trial design can better evaluate the effect of the quality improvement intervention on care and outcomes while minimizing potential biases.[9,26]

Previous cluster-randomized studies of AIS that utilized different quality improvement tools showed mixed results. The Project for the Improvement of Stroke Care Management in Minnesota (PRISMM) failed to identify a quality improvement intervention effect in care. Only 5 of 10 performance measures were the same with those in this trial. The quality improvement tools were also different from those in this trial. In particular, control hospitals in the PRISMM study also received audit and written feedback of baseline performance, which helped to improve quality.[14] However, cluster-randomized studies demonstrated that clinical pathways can significantly increase evidence-based management procedures, such as early aspirin prescription and dysphagia screen.[12,27] Implementation of standardized discharge orders after stroke is also associated with improved optimal secondary stroke prevention.[15] The Increasing Stroke Treatment Through Interventional Behavioral Change Tactics (INSTINCT) trial used a multifaceted intervention, such as a clinical practice guideline promotion, telephone support for treatment decisions, and audit and feedback mechanisms. The trial demonstrated significant improvement in the use of alteplase in eligible patients.[13] It is possible that the frequency of measuring quality indicators might have influenced the quality of stroke care. Physicians may improve their behavior in response to their awareness of being observed, a phenomenon known as the Hawthorne effect,[28] which may be a part of the quality improvement initiative intervention.

There were several important considerations incorporated in this trial. A cluster-randomized design reduced the likelihood of contamination between intervention and control groups of the trial. Concealed allocation and blind adjudication of outcomes were used to avoid bias.[29] The use of intention-to-treat principles prompted the use of a cluster design to minimize the risk of biased selection of reporting of the outcomes. In addition, the data were collected by trained independent research coordinators at each hospital who were independent of the care processes. The HR curves of these new clinical vascular events were almost completely separated in the first 30 days. Adherence to secondary stroke prevention therapy can reduce cardiovascular events as identified in the randomized trials and by recommended international guidelines.[4,5,19,30] Meanwhile, other findings included that the long-term disability was lower in the intervention group than that in the control group, which may contribute to the decrease of new clinical vascular events, especially recurrent stroke. Evidently, the favorable outcomes

Table 3. New Vascular Events, Disability, and Death Among Patients With Acute Ischemic Stroke Receiving a Multifaceted Quality Improvement Intervention (Intervention) vs Routine Care + Stroke Registry Participation Group (Control) in China

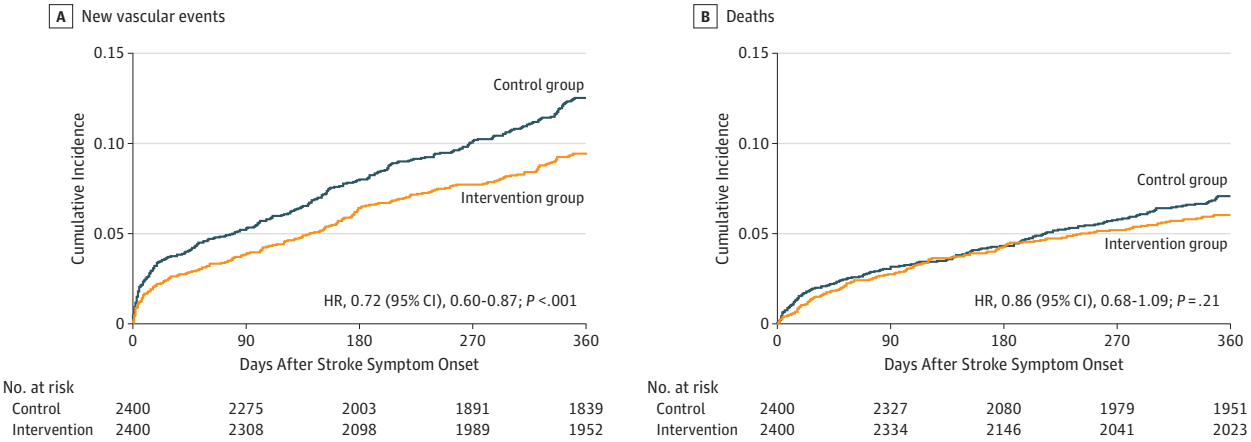
	Intervention, No. of Events/Total Patients (%)	Control, No. of Events/Total Patients (%)	Absolute Difference (95% CI), %[a]	*P* Value	Hazard Ratio (95% CI)[a]	Odds Ratio (95% CI)[a,b]	*P* Value
New vascular events							
3 mo	93/2400 (3.9)	127/2400 (5.3)	−2.0 (−3.5 to −0.6)	.007	0.65 (0.49 to 0.86)		.002
6 mo	150/2400 (6.3)	186/2400 (7.8)	−2.2 (−4.0 to −0.4)	.02	0.72 (0.57 to 0.90)		.004
12 mo	218/2400 (9.1)	282/2400 (11.8)	−3.1 (−5.3 to −1.0)	.005	0.72 (0.60 to 0.87)		<.001
Disability (mRS, 3-5)							
3 mo	418/2180 (19.2)	443/2105 (21.0)	−3.7 (−6.7 to −0.8)	.01		0.76 (0.63 to 0.91)	.002
6 mo	326/2058 (15.8)	360/2009 (17.9)	−3.9 (−6.6 to −1.1)	.006		0.74 (0.61 to 0.89)	.002
12 mo	236/1852 (12.7)	264/1798 (14.7)	−3.1 (−5.8 to −0.5)	.02		0.74 (0.59 to 0.93)	.01
Death							
In hospital	11/2400 (0.5)	23/2400 (1.0)	−0.7 (−1.1 to 0.2)	.009	0.96 (0.90 to 1.02)		.14
3 mo	66/2400 (2.8)	76/2400 (3.2)	−1.0 (−2.1 to 0.1)	.08	0.81 (0.57 to 1.15)		.23
6 mo	103/2400 (4.3)	101/2400 (4.2)	−0.5 (−1.7 to 0.6)	.38	0.97 (0.73 to 1.29)		.81
12 mo	139/2400 (5.8)	160/2400 (6.7)	−1.5 (−3.0 to −0.0)	.05	0.86 (0.68 to 1.09)		.21

Abbreviation: mRS, modified Rankin Scale.

[a] Adjusted for patient and hospital characteristics, including age, sex, history of ischemic stroke, hypertension disease, diabetes, hyperlipidemia, atrial fibrillation, coronary artery disease and previous myocardial infarction, ever smoking, National Institutes of Health Stroke Scale score at admission, hospital grade, region, stroke unit, teaching hospital status, and No. of neurological ward beds.

[b] Disability was measured by mRS score (range, 3-5) to describe the function status at 3, 6, and 12 mo after stroke onset. A mixed-model with a binary link function was used to analyze the disability and odds ratio was calculated to demonstrate the benefit of intervention group on patient's function status.

Figure 2. New Vascular Events and Death at 12-Month Follow-up Among Patients Hospitalized With Acute Ischemic Stroke Implementing Multifaceted Quality Improvement Intervention (Intervention) vs Routine Care + Stroke Registry Participation Group (Control) in China



HR indicates hazard ratio. The median time of follow-up was 364 days (interquartile range [IQR], 364-365) in the intervention group and 365 days (IQR, 364-365) in the control group. The log-rank test was used to compare the days after stroke symptom onset to the occurrence of new clinical vascular events or death.

associated with increased adherence to evidence-based performance measures should be interpreted with caution. In these findings, the clinical effect size is much greater than the process effect size. One possible explanation of this observation is that the intervention itself may have improved overall stroke care, not just the process measures. Patient benefit from the intervention may be only partially captured by improved process measures. In addition, the significant effect of the intervention was preserved when a sensitivity analysis did not exclude any patients with a documented contraindication, suggesting that the benefit was due to more patients getting the intervention rather than more documentation of exclusions.

Limitations

This trial had several limitations. First, the difference of composite score between the 2 groups is 3.4%, which was smaller than the minimal detectable differences used in the power analysis (5% improvement). Second, those hospitals enrolled from the China National Network of Stroke Research may be more motivated and have greater access to resources to improve stroke care quality than other hospitals. Further studies will be necessary to determine the effect of this quality improvement intervention in hospitals in China that differ in characteristics from those that participated. Third, the quality improvement intervention was studied over an 11-month period and additional study is needed to determine whether improvement in stroke care would continue over a longer period and whether differences in mortality may emerge with follow-up beyond 1 year. Fourth, the selected quality improvement measures in this trial were limited to medical management of stroke. Other quality improvement measures in stroke, such as rehabilitation evaluation and treatment, stroke education, and smoking cessation counseling, were not evaluated. Fifth, these interventions are hospital-based, and adherence after hospital discharge can affect the benefits. Additional strategies should be considered to reduce secondary vascular events after discharge.[31] Sixth, leaving the hospital against medical advice is an important factor that affects outcomes of patients with stroke after discharge. This information was not recorded in this study. Seventh, imputing missing data on smoking as all "nonsmoking" is another limitation.

Conclusions

Among 40 hospitals in China, a multifaceted quality improvement intervention compared with usual care resulted in a statistically significant but small improvement in hospital personnel adherence to evidence-based performance measures in patients with acute ischemic stroke when assessed as a composite measure, but not as an all-or-none measure. Further research is needed to understand the generalizability of these findings.

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