

GWTG Risk Model for All Stroke Types Predicts In-Hospital and 3-Month Mortality in Chinese Patients with Acute Stroke

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Background: We aimed to externally validate the Get With the Guidelines (GWTG) risk model for all stroke types to predict in-hospital stroke mortality in Chinese patients and moreover to explore its prognostic value in predicting 3-month mortality after stroke. *Methods:* The prognostic model was applied to patients with acute stroke from China National Stroke Registry II (CNSR II) to predict in-hospital and 3-month mortality. Model discrimination was estimated by calculating c-statistic and 95% confidence intervals (CIs). Calibration was assessed by Pearson correlation coefficient and Hosmer-Lemeshow test. *Results:* Data from 21,684 stroke patients with complete data for in-hospital mortality prediction and 20,348 stroke patients with complete data for 3-month mortality prediction in the CNSR II were abstracted. The in-hospital and 3-month mortality were 1.4% and 5.6%, respectively. The c-statistics in the CNSR II were .86 (95% CI, .84-.88) and .83 (95% CI, .81-.84) for in-hospital and 3-month mortality, respectively. Calibration plot presented high correlation between the observed and predicted mortality rates (Pearson correlation coefficient, .996 for in-hospital and .998 for 3-month mortality; both $P < .001$). The Hosmer-Lemeshow statistics for the prediction of in-hospital and 3-month mortality were 0.21 and less than .001, respectively. The model performed nearly as well in each stroke type as in the overall model including all types. *Conclusions:* The GWTG risk model for all stroke types is a valid clinical tool to predict in-hospital and 3-month mortality in Chinese patients with acute stroke of any type.

Key Words: Stroke—prognosis—mortality—outcomes—risk factors

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Introduction

Stroke is the second leading cause of death globally¹ and the first leading cause of death in China.² A considerable portion of stroke deaths occur during hospitalization.

The risk of death varies greatly according to stroke types, with higher mortality in intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) compared with ischemic stroke (IS).³ A tool to predict mortality from all forms of stroke is useful in many ways such as

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determining prognosis, making treatment plan, and assessing medical care quality based on patient case mix.

However, most previous in-hospital mortality-predicting models were setting-specific for a single type of stroke,⁴⁻¹¹ which made them inconvenient to implement in stroke of all types. Smith et al¹² developed and internally validated more general predictive models for in-hospital mortality from acute stroke of any type (IS, ICH, SAH, or uncertain type) based on Get With the Guidelines-Stroke (GWTG-Stroke) database, of which, a risk score incorporating National Institutes of Health Stroke Scale score (GWTG risk model for all stroke types) showed excellent discrimination and calibration. However, its usefulness in Chinese patients with acute stroke is still unknown.

The purpose of the current study was to validate the performance of the GWTG risk model for all stroke types in different stroke populations in the China National Stroke Registry II (CNSR II) and moreover to explore its prognostic value in predicting 3-month mortality after stroke.

Methods

Study Population

The data set was derived from the CNSR II, the design, rationale, and baseline information of which had been published elsewhere.¹³ In brief, CNSR II was a nationwide prospective cohort study of consecutive patients with acute stroke within 7 days after the onset of symptoms from June 2012 to January 2013 in China. A total of 219 hospitals from different regions representing 27 provinces and 4 municipalities in mainland China were selected. Detailed demographic and clinical data were collected by trained research coordinators with standardized data collection tool.

The protocol and data collection was approved by the Institutional Review Board at Beijing Tiantan Hospital and all participating hospitals. Written informed consents were obtained from all participants or their designated relatives.

The diagnosis¹⁴ and classification¹⁵ of acute stroke was made according to WHO criteria combined with brain computed tomography or magnetic resonance imaging confirmation. For the current study, we included acute stroke of any type (IS, ICH, SAH, and uncertain type).

Variable Definition and Data Collection

Variables for GWTG risk model included age, gender, initial National Institutes of Health Stroke Scale Score, mode of arrival (ambulance from scene, private transport, and did not present via emergency department), medical history (history of atrial fibrillation, previous stroke/transient ischemic attack, coronary artery disease, peripheral vascular disease, and dyslipidemia), time of arrival

(7 AM-5 PM from Monday to Friday as daytime regular hours), and stroke type. Data were derived from the CNSR II database according to the definitions in the original article.¹² Patients were excluded if any of the variables above were not available.

Outcome Measures

The main outcomes of interest were in-hospital and 3-month death. A death certificate from the local citizen registry or the attended hospital was used to confirm the in-hospital case fatality. Death at 3 months was assessed by trained study investigators through telephone interview at 3 months, which was centralized with a standardized interview protocol.

Statistical Analyses

Baseline characteristics were expressed as mean (standard deviation) or median (interquartile range) for continuous variables and as percentages for categorical variables. Student *t* test or Kruskal-Wallis test for continuous variables and χ^2 test for categorical variables were used as needed. The calculation of the mortality and risk score category were performed in a manner identical to that reported in the original article.¹² The discrimination of the model (c-statistic) was assessed by the area under the receiver-operator curves and 95% confidence intervals (CIs). Calibration was assessed by Pearson correlation coefficient (*r*) and Hosmer-Lemeshow test. The observed and predicted mortality rates were plotted with 10 deciles of predicted risk. The discrimination and calibration of the model for each individual stroke type were also assessed.

A 2-sided *P* value less than .05 was set as the level for statistical significance. All analyses were performed with SAS software version 9.4 (SAS Institute Inc, Cary, NC).

Results

Between 2012 and 2013, there were 25,018 patients with acute stroke registered in CNSR II. After excluding 3334 patients with missing data on mode of arrival, a total of 21,684 eligible patients (IS, 86.5%; ICH, 11.9%; SAH, 1.2%; and uncertain type, .4%) were included in the analysis for in-hospital mortality prediction. The in-hospital mortality data were completed. After excluding 1336 patients lost 3-month follow-up, 20,348 patients were included in the analysis for 3-month mortality prediction (Supplementary Figure 1 in the online-only Data Supplement).

The ages of the participants in the analysis for in-hospital mortality prediction ranged from 18 to 99 years (mean 64 ± 12 years) and 62.8% were male. The median length of hospital stay was 13 days (interquartile range 9-16). Mortality rates for the CNSR II were 1.4 % (295 deaths) during hospitalization and 5.6% (1134 deaths) at 3 months. In-hospital and 3-month mortality varied

according to stroke types (in-hospital mortality: IS, 1.1%; ICH, 3.8%; SAH, 5.1%; uncertain type, 1.2%; and $P < .001$; 3-month mortality: IS, 4.8%; ICH, 12.9%; SAH, 14.9%; uncertain type, 8.6%; and $P < .001$). The patients in CNSR II were quite different from those in GWTG database in demographic and clinical characteristics (Table 1). Chinese patients were younger, more likely to be male, less likely to present via ED, had less stroke severity and lower in-hospital mortality.

The risk of death increased by increasing points of the model, from .2 % with point of 0-20 to 50.0% with point greater than 100 for in-hospital mortality rate, and from .8% with point of 0-20 to 83.3% with point greater than 100 for 3-month mortality rate (Fig 1).

The GWTG risk model displayed good discriminatory power in CNSR II, the c-statistics were .86 (95% CI, .84-.88) for in-hospital mortality prediction and .83 (95% CI, .81-.84) for 3-month mortality prediction (Fig 2), respectively. Calibration plot presented high correlation between the observed and predicted mortality rates (r , .996 for in-hospital mortality and .998 for 3-month mortality, both $P < .001$; Fig 3). The significance levels of the Hosmer-Lemeshow test for the prediction of in-hospital and 3-month mortality were .21 and less than .001, respectively.

The discrimination and calibration of the model for in-hospital and 3-month mortality rates within each individual stroke type (IS, ICH, and SAH) were also excellent (Table 2).

Discussion

Our study showed that the GWTG risk model for all stroke types was able to reliably predict the in-hospital mortality in patients with acute stroke of all types in China, even the Chinese patients were significantly different in baseline characteristics from those in the United States. Moreover, we extended for the first time the prognostic role of the GWTG risk model for all stroke types to predict 3-month mortality rate after acute stroke in Chinese patients. Besides, the prognostic utility of this model for each individual stroke type was also excellent.

The calibration of the GWTG risk model for all stroke types appeared excellent, with high correlations between observed and predicted event rates. However, we noticed that the Hosmer-Lemeshow test was significant for some models including models for predicting 3-month mortality in stroke of all types, IS alone and ICH alone and for predicting in-hospital mortality in ICH alone, which indicated a significant difference between the observed and predicted event rates. The possible explanation for this discrepancy could be as follows. First, the Hosmer-Lemeshow test was oversensitive to trivial deviations from good fit in large samples¹⁶ and thus presented excessively high statistical power since there were as many as 21,684 patients included in the analyses. Second, the treatment changes with time may affect the outcome. The original risk model was constructed based on the stroke patients' data between 2001 and 2007 while the data of the Chinese

Table 1. Patient characteristics in GWTG and CNSR II Data Sets

Main characteristics	GWTG data (n = 333,865)	CNSR II data (n = 21,684)	P value
Age (year), mean \pm SD	71.1 \pm 14.7	64.3 \pm 12.1	<.001
Male gender, %	46.7	62.8	<.001
Initial NIHSS Score, median (IQR)	5 (2-11)	4 (1-7)	<.001
<i>Mode of arrival, %</i>			
EMS from scene	54.7	18.8	<.001
Private transport	39.1	34.9	<.001
Did not present via ED	6.2	46.2	<.001
<i>Medical history, %</i>			
Atrial fibrillation	17.5	6.1	<.001
Previous stroke/TIA	29.6	34.6	<.001
Coronary artery disease	26.4	2.2	<.001
Peripheral vascular disease	4.9	4.0	<.001
Dyslipidemia	33.3	11.1	<.001
Arrived daytime regular hours*, %	45.7	43.5	<.001
<i>Stroke type, %</i>			
Ischemic stroke	82.4	86.5	<.001
Subarachnoid hemorrhage	2.6	1.2	<.001
Intracerebral hemorrhage	11.2	11.9	.001
Stroke of uncertain type	3.8	0.4	<.001
Died in the hospital, %	8.5	1.4	<.001

Abbreviations: CNSR II, China National Stroke Registry II; ED, emergency department; EMS, emergency medical services; GWTG data, Get With the Guidelines-Stroke database; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; TIA, transient ischemic attack.

*Daytime regular hours were defined as 7 AM to 5 PM Monday to Friday; all other times (including all-day Saturday and Sunday) were considered off-hours.

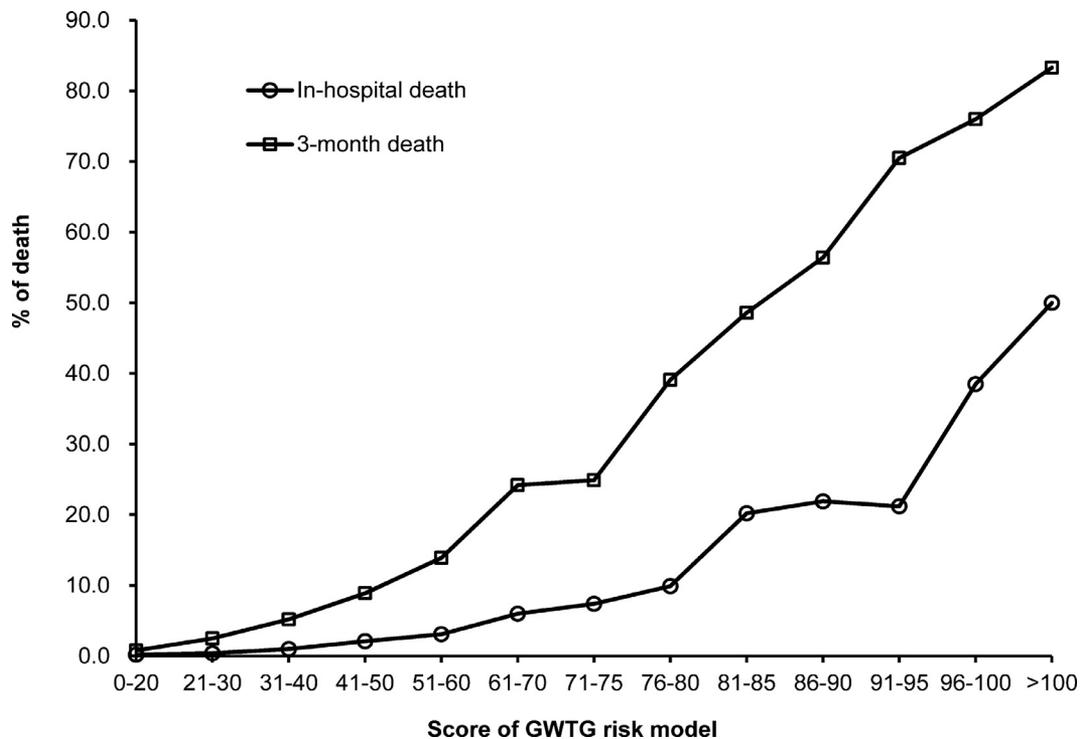


Figure 1. In-hospital and 3-month mortality rates in China National Stroke Registry II according to risk score category.

patients were captured between 2012 and 2013.^{12,13} There are differences in the stroke treatments between these 2 periods, especially the time window of tPA and endovascular treatment.¹⁷⁻¹⁹ Third, missing data may have influenced the result since 1336 patients were excluded for lacking 3-month follow-up, which is nearly the same size as 3-month deaths. Whether the treatment changes or data exclusion could influence the results needs to be validated in future studies. Although the model discrimination and Pearson correlation coefficient seems good, the possibility of inaccurate prediction may not be ruled out when we predict 3-month mortality in stroke of all types, IS alone and ICH alone and in-hospital mortality in ICH alone at present.

Most previous mortality-predicting models⁴⁻¹¹ were setting-specific for a single type of stroke, which meant the clinicians had to assess the mortality in all forms of stroke with several predicting models. The GWTG risk model for all types of stroke could solve this problem in 1 model and present excellent prognostic utility for each individual stroke type, in the population of either United States or China.

The GWTG risk model for all stroke types can be used in many aspects including providing prognostic information to patients and their families, aiding clinicians in treatment planning for patients at risks, and helping medical institutions facilitate better quality of care through identifying the correlation between actual stroke case fatality rates and predicted rates based on patient case mix. This model was designed only with simple variables

present on hospital admission and routinely recorded by clinicians in China, which allowed it to be easily used at the time of admission to predict in-hospital and 3-month mortality and thus to aid clinical care. Moreover, independent of imaging data and specialized laboratory tests, it was easy to use at small centers with limited resources to estimate mortality after stroke.

To our knowledge, this is the first external validation study for the GWTG risk model for all stroke types through a different independent population from China. In addition, using the postdischarge information in CNSR II database, we extended prognostic role of the GWTG risk model for all stroke types to predict 3-month mortality after acute stroke.

This study has certain limitations. First, it is based on a prospective study, bearing the limitations of such study design. Exclusion of patients from mortality prediction and treatment changes between the 2 data sets may have influenced the results, which need to be validated in future studies. Second, the participating centers in the CNSR II might represent the institutes with more resources and expertise than those in rural areas, which could produce a selection bias. Therefore, the risk of death in the Chinese population might have been underestimated. However, this enrollment bias should not affect the accuracy of the GWTG risk model for all stroke types as an integral predictive tool. Third, we failed to individually validate the performance of this model for in-hospital mortality in stroke of uncertain type alone, owing to its small sample size (86 cases, .4%, 1 case dead in hospital) in CNSR II.

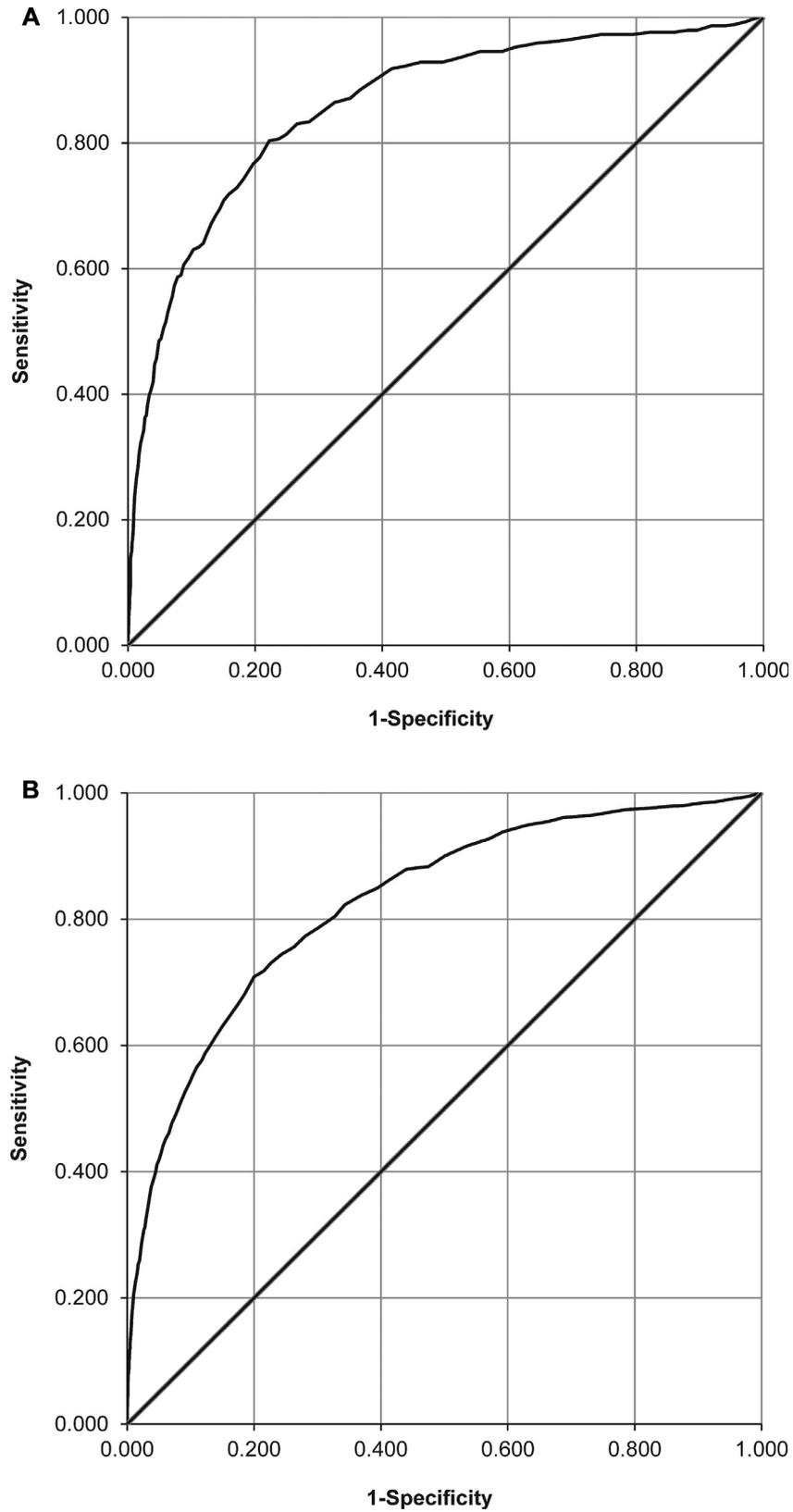


Figure 2. Receiver-operator curve of the Get With the Guidelines risk model for all stroke types in China National Stroke Registry II cohort for in-hospital mortality prediction (A) and 3-month mortality prediction (B). The c-statistics was .86 (95% CI, .84-.88) for in-hospital mortality prediction and .83 (95% CI, .81-.84) for 3-month mortality prediction. Abbreviation: CI, confidence interval.

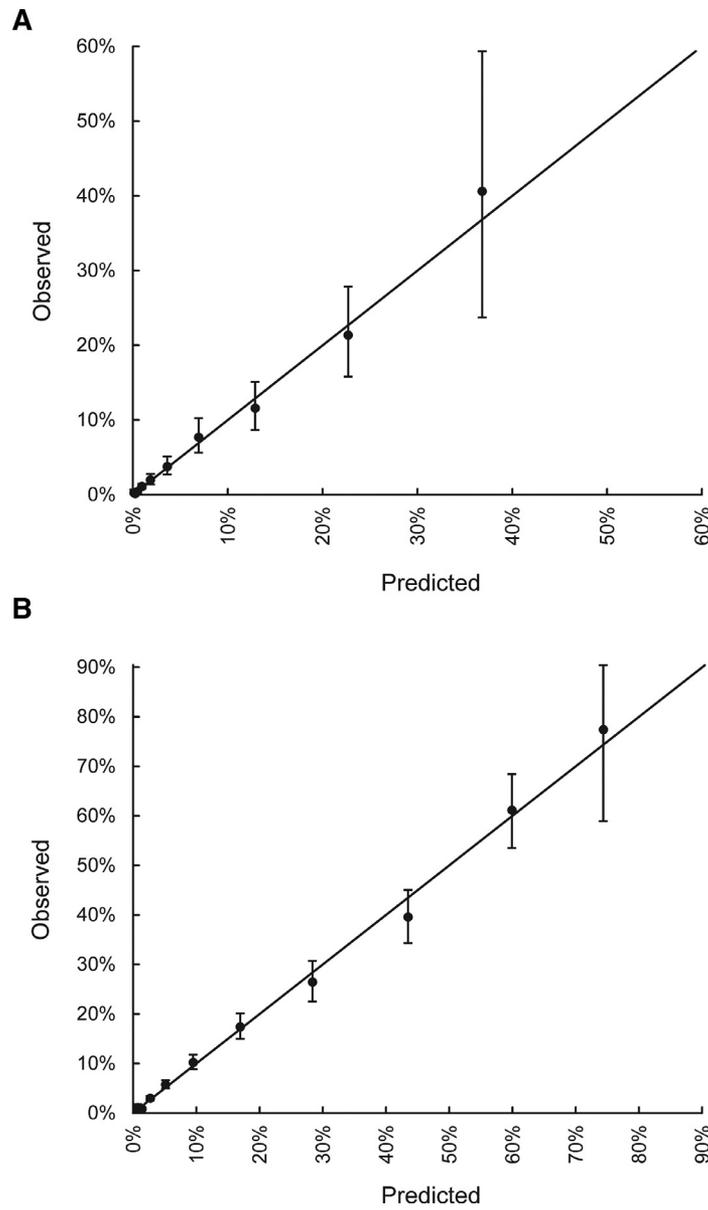


Figure 3. Observed versus predicted in-hospital mortality (A) and 3-month mortality (B) in the validation sample (Pearson correlation coefficient, .996 for in-hospital mortality and .998 for 3-month mortality, both $P < .001$).

Table 2. Model discrimination and calibration in each stroke type

	All	IS alone	ICH alone	SAH alone	Uncertain type alone
<i>In-hospital</i>					
c-statistic	.86	.85	.80	.86	-
r	.996	.837	.987	.832	-
P value	<.001	.005	<.001	.02	-
H-L Statistic	.21	.44	.01	.89	-
<i>3-Month</i>					
c-statistic	.83	.82	.83	.71	.79
r	.998	.942	.995	.906	.852
P value	<.001	<.001	<.001	.005	.01
H-L Statistic	<.001	.001	.02	.16	.50

Abbreviations: H-L statistic, Hosmer-Lemeshow statistic; ICH, intracerebral hemorrhage; IS, ischemic stroke; r, Pearson correlation coefficient; SAH, subarachnoid hemorrhage.

Conclusions

In conclusion, the GWTG risk model for all stroke types is a valid clinical tool to predict in-hospital and 3-month mortality in Chinese patients with acute stroke of any type.

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Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2018.11.024.

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