# **ARTICLE IN PRESS**

# External Validation of the Prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale Score for Predicting Pneumonia After Stroke Using Data From the China National Stroke Registry

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Background and purpose: Pneumonia is an important risk factor for mortality and morbidity after stroke. The Prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale (ISAN) score was shown to be a useful tool for predicting stroke-associated pneumonia based on UK multicenter cohort study. We aimed to externally validate the score using data from the China National Stroke Registry (CNSR). Methods: Eligible patients with acute ischemic stroke (AIS) and intracerebral hemorrhage (ICH) in the CNSR from 2007 to 2008 were included. The area under the receiver operating characteristic (AUC) curve was used to evaluate discrimination. The Hosmer-Lemeshow goodness of fit test and Pearson correlation coefficient were performed to assess calibration of the model. Results: A total of 19,333 patients (AIS = 14400; ICH = 4933) were included and the overall pneumonia rate was 12.7%. The AUC was .76 (95% confidence interval [CI]: .75-.78) for the subgroup of AIS and .70 (95% CI: .68-.72) for the subgroup of ICH. The Hosmer-Lemeshow test showed the ISAN score with the good calibration for AIS and ICH (P = .177 and .405, respectively). The plot of observed versus predicted pneumonia rates suggested higher correlation for patients with AIS than with ICH (Pearson correlation coefficient = .99 and .83, respectively). Conclusions: The ISAN score was a useful tool for predicting in-hospital pneumonia after acute stroke, especially for patients with AIS. Further validations need to be done in different populations. Key Words: Stroke—pneumonia—ISAN score—intracerebral hemorrhage.

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## Introduction

Pneumonia is a common in-hospital medical complication after stroke, and the overall incidence was 14.3% from a recent meta-analysis. Several studies have suggested that stroke-associated pneumonia (SAP) is an important risk factor for medical cost, length of hospital stay, as well as morbidity and mortality after stroke. <sup>2-6</sup>

Several risk scores have been developed to predict SAP, such as the Age, Atrial fibrillation, Dysphagia, Sex, Stroke Severity (A<sup>2</sup>DS<sup>2</sup>) score, the acute ischemic stroke-associated pneumonia score (AIS-APS), the intracerebral hemorrhage-associated pneumonia score (ICH-APS), etc. These scores were useful tools for predicting pneumonia after acute ischemic stroke (AIS), or grading risk of pneumonia after intracerebral hemorrhage (ICH).<sup>7-11</sup> Recently, a refined prediction score, named ISAN (prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale), was derived and validated in a multicenter UK cohort.<sup>12</sup> Compared with prior risk scores, the ISAN score, with only 4 predictors, is simpler for predicting SAP in routine practice.

However, the ISAN score has just been validated in a European study and its utility for different population is not known. Meanwhile, with so many predicting models existing, which one is more precision, practicable, and useful in clinical practice? The purpose of this study is to validate the ISAN score in Asian population, and to compare the discrimination of the ISAN score with the A<sup>2</sup>DS<sup>2</sup> score, AIS-APS, and ICH-APS for SAP.

### Methods

## Patients Selection

Patients with AIS and ICH from the China National Stroke Registry (CNSR) were identified in this validation. Full detailed information on the CNSR had been published previously.<sup>13</sup> Briefly, CNSR was national prospective cohort, in which patients with cerebrovascular events within 14 days were enrolled from 132 hospitals between September 2007 and August 2008 in China. Paperbased standard registry forms were used to collect relevant information. Trained research coordinators gained prestroke modified Rankin scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) by face-to-face interview, and participant demographics and vascular risk factors were collected through medical records. The CNSR protocol was approved by the central Ethics Committee at Beijing Tiantan Hospital and each Institutional Review Board of participating hospitals. All patients enrolled had signed written consent by themselves or their legal representatives. All data were de-identified prior to access.

### Data Definitions

In the present study, the variables used to calculate ISAN score included sex (0 score for female, 1 score for male),

age (<60 years assign 0 score, 60 to 69 years assign 3 scores, 70 to 79 years assign 4 scores, 80 to 89 years assign 6 scores,  $\geq$ 90 years assign 8 scores), prestroke independence (0 score for mRS 0 to 1, 2 scores for mRS 2 to 5), and NIHSS (0 score for 0 to 4, 4 scores for 5 to 15, 8 scores for 16 to 20, 10 scores for  $\geq$ 21). The 22-point ISAN score was stratified into 4 risk classes of SAP, with low risk (score 0 to 5), medium risk (score 6 to 10), high risk (score 11 to 14), and highest risk (score more than 15).

For other related score systems, we computed the A2DS2 score, AIS-APS, and ICH-APS according to original studies.<sup>9-11</sup> Age (<75 years assign 0 point, ≥75 years assign 1 point), atrial fibrillation (0 point for no, 1 point for yes), dysphagia (0 point for no, 2 points for yes), sex (0 point for female, 1 point for male), and stroke severity (0 point for NIHSS 0 to 4, 3 points for NIHSS 5 to 15, 5 points for NIHSS ≥16) were used to assign each patient the A<sup>2</sup>DS<sup>2</sup> score. To calculate the AIS-APS, 11 variables were used, including age (0 score for age ≤59, 2 scores for age 60 to 69, 5 scores for age 70 to 79, 7 scores for age ≥80), medical history (1 score for atrial fibrillation, 3 scores for congestive heart failure, 3 scores for chronic obstructive pulmonary disease, 1 score for current smoking), prestroke dependence (2 scores for mRS ≥3), admission NIHSS score (0 score for NIHSS 0 to 4, 2 scores for NIHSS 5 to 9, 5 scores for NIHSS 10 to 14, 8 scores for NIHSS ≥15), admission Glasgow Coma Scale (GCS) (3 scores for GCS 3 to 8, 0 score for GCS 9 to 15), symptom of dysphasia (3 scores for dysphasia), Oxfordshire Community Stroke Project (OSCP) subtype (0 score for lacunar infarction or partial anterior circulation infarct, 2 scores for total anterior circulation infarct or posterior circulation infarct), and admission glucose (≤11.0 mmol/L assign 0 score, ≥11.1 mmol/L assign 2 scores). The variables in ICH-APS included age (0 score for age ≤59, 2 scores for age 60 to 69, 3 scores for age 70 to 79, 5 scores for age ≥80), current smoking (0 score for nonsmoking, 1 score for smoking), excess alcohol consumption (0 score if no, 1 score if yes), chronic obstructive pulmonary disease (0 score if no, 1 score if yes), prestroke dependence (2 scores for mRS ≥3), admission GCS score (0 score for GCS 15, 2 scores for GCS 3 to 14), admission NIHSS score (0 score for NIHSS 0 to 5, 1 score for NIHSS 6 to 10, 2 scores for NIHSS 11 to 15, 3 scores for NIHSS ≥16), dysphagia (0 score for no, 1 score for yes), infratentorial location (0 score for no, 1 score for yes), and extension into ventricles (0 score for no, 1 score for yes).

In the prior 3 score systems, dysphasia was defined as any symptom of dysphasia, including any tests of dysphasia screening. Excess alcohol consumption was defined as ≥2 standard alcohol beverage per day.

#### Outcome Measures

The outcome of concern was in-hospital SAP after acute stroke. In this registry, SAP was diagnosed by treating

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