External Validation of the Prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale (ISAN) Score for Predicting Stroke-Associated Pneumonia in the Athens Stroke Registry

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Background and purpose: The Prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale (ISAN) score was developed recently for predicting stroke-associated pneumonia (SAP), one of the most common complications after stroke. The aim of the present study was to externally validate the ISAN score. *Methods:* Data included in the Athens Stroke Registry between June 1992 and December 2011 were used for this analysis. Inclusion criteria were the availability of all ISAN score variables (prestroke independence, sex, age, National Institutes of Health Stroke Scale score). Receiver operating characteristic curves and linear regression analyses were used to determine the discriminatory power of the score and to assess the correlation between actual and predicted pneumonia in the study population. Separate analyses were performed for patients with acute ischemic stroke (AIS) and intracerebral hemorrhage (ICH). *Results:* The analysis included 3204 patients (AIS: 2732, ICH: 472). The ISAN score demonstrated excellent discrimination in patients with AIS (area under the curve [AUC]: .83 [95% confidence

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interval {CI}: .81-.85]). In the ICH group, the score was less effective (AUC: .69 [95% CI: .63-.74]). Higher-risk groups of ISAN score were associated with an increased relative risk of SAP; risk increase was more prominent in the AIS population. Predicted pneumonia correlated very well with actual pneumonia (AIS group: $R^2 = .885$; β-coefficient = .941, $P < .001$; ICH group: $R^2 = .880$, β-coefficient = .938, $P < .001$). *Conclusions:* In our external validation in the Athens Stroke Registry cohort, the ISAN score predicted SAP very accurately in AIS patients and demonstrated good discriminatory power in the ICH group. Further validation and assessment of clinical usefulness would strengthen the score's utility further. **Key Words:** ISAN score—pneumonia—stroke—intracerebral hemorrhage—prediction—outcome.
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Introduction

The incidence of pneumonia after stroke ranges between 1% and 44%.[1,2] Regardless of the exact percent, which depends highly on the heterogeneity of the performed studies, pneumonia is widely recognized as one of the most frequent medical complications of stroke.[3] Stroke-associated pneumonia (SAP) has a detrimental impact on survival (threefold increased risk of 30-day mortality after adjusting for admission severity and propensity for pneumonia),[4] healthcare costs (3.5-fold increase in hospitalization cost and 70% more likely to require extended care post discharge),[5] and, in most studies, functional outcome.[6-9] Therefore, the ability to predict the risk of SAP could aid in targeting interventions to reduce SAP risk to the patients at highest risk (improved patient outcomes in daily clinical practice and stroke logistics) and to facilitate more appropriate patient selection for clinical trials of preventative or therapeutic interventions.

Despite the high significance of SAP, attempts to build and widely validate a rapidly calculated and accurate prognostic score are quite limited,[10-16] in comparison to scores related to other stroke outcomes.[17-19] Prestroke Independence, Sex, Age, National Institutes of Health Stroke Scale (ISAN), the most recently introduced score in this category, was developed and internally validated in a national UK cohort of patients with stroke.[13] The score had a similar accuracy in the 2 cohorts, but its discriminatory power was higher in the acute ischemic stroke (AIS) group than in the intracerebral hemorrhage (ICH) group.

The aim of the present study was to externally validate the ISAN score in the Athens Stroke Registry, a prospectively collected stroke population of AIS and ICH patients recorded under different geographical, temporal, and socioeconomic circumstances.

Materials and Methods

Study Population and Definitions

All consecutive patients with a first-ever stroke (AIS or ICH) registered in the Athens Stroke Registry (ASR) between June 1992 and December 2011 were included in the present study. The ASR is the prospective registry of all patients with first-ever strokes admitted in Alexandra University Hospital (Athens, Greece). By definition, transient ischemic attacks, subarachnoid hemorrhages, and recurrent strokes are not included in the ASR. All patients have been treated according to current international guidelines at the time of admission. The clinical settings, the definition of variables, the diagnostic algorithms applied, and the way data were collected and recorded have been previously described.[20,21]

The ISAN score was calculated on the basis of prestroke **I**ndependency (0 points for modified Rankin Scale [mRS] score = 0-1, 2 points for mRS score = 2-5), **S**ex (1 point for males, 0 points for females), **A**ge (0 points if <60 years, 3 points if 60-69 years, 4 points if 70-79 years, 6 points if 80-89 years, and 8 points if ≥90 years) and **N**ational Institutes of Health Stroke Scale (NIHSS) score on admission (0 points if 0-4, 4 points if 5-15, 8 points if 16-20, and 10 points if ≥21).[13] The patients were stratified for their risk of pneumonia into low risk (ISAN score: 0-5), medium risk (6-10), high risk (11-14), and very high risk (≥15).[13]

Pneumonia was diagnosed according to the individual judgment of the treating physician, based on the presence of respiratory tract infection symptoms or signs (fever, cough, crackles in lung auscultation, or/and changes in expectoration), laboratory test results (increase of inflammatory markers, reduced oxygen saturation, or/and pathogen detection in sputum cultures), and typical radiological evidence. Pneumonia was considered as SAP if it presented during the patients' hospitalization for the stroke. Time delay to SAP onset was arbitrarily defined as the time window from the patient's admission to the first recording (temporally related to SAP) of body temperature less than 37.5°C.

Inclusion criteria were the availability of the prerequisite variables for the calculation of ISAN score and assessment of the patient for the development of pneumonia during hospitalization. No specific exclusion criteria were applied.

The Institutional Ethics Committee has approved the scientific use of the data collected in the ASR.

Statistical Analysis

Data were analyzed separately for AIS and ICH patients. Continuous covariates are summarized as median

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