VOL. 4, NO. 4, 2024
ISSN 2772-3747

Letters

RESEARCH LETTER

Developing and Validating a Risk Score for Predicting 1-Year Serious Adverse Events After Syncope

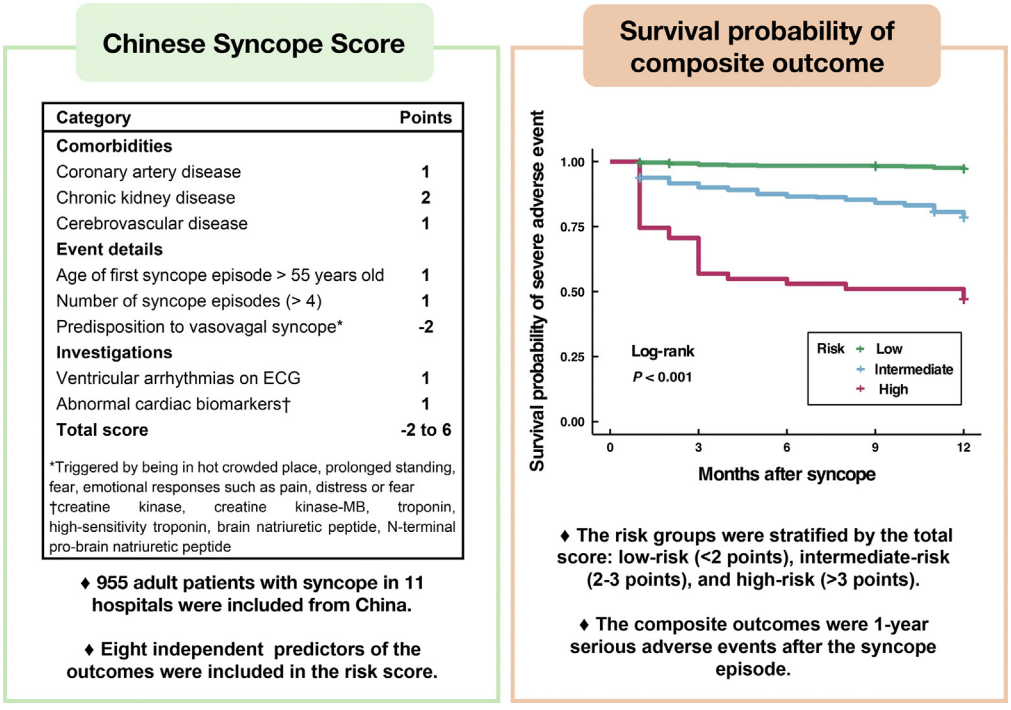
Syncope is a transient loss of consciousness due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery. It has been emphasized that risk stratification during initial evaluation is critical for guiding management and preventing long-term morbidity and mortality. Several syncope clinical decision scores have been developed to predict short- or long-term serious outcomes, but none are specific for Asians.[1] This study aimed to evaluate the risk of 1-year serious adverse events after a syncope episode in a Chinese prospective multicenter cohort.

We used the data from the Multicenter Registration Study for Syncope Patients in China. Consecutive adult patients (age ≥18 years) with syncope were enrolled from June 1, 2018, to February 28, 2022, with follow-up conducted until 2023. The initial evaluation of the patients was performed by an independent researcher, and the final diagnosis was identified. The study was approved by the Ethics Committee of the Peking University People's Hospital and adhered to the 2000 revised Declaration of Helsinki.

Risk prediction and score models were conducted and reported after the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis) guideline.[2] The composite outcome included any of the following events: all-cause death, arrhythmia, myocardial infarction, serious structural heart disease, aortic dissection, pulmonary embolism, severe hemorrhage, stroke, cerebral hemorrhage, and any other serious condition and procedural intervention associated with syncope. Based on the literature review and clinical variables associated with syncope risk stratification, 31 candidate predictors were selected that may contribute to model development. To identify independent predictors, we included candidate predictors with $P < 0.05$ in the univariate Cox regression model in a multivariable Cox regression model, using backward stepwise selection ($P < 0.05$). A weighted risk score was derived for each patient by summing the integer assigned to each predictor by dividing each β coefficient by the smallest β coefficient and rounding to the nearest integer. Discrimination and calibration were assessed using C statistic and calibration slope, respectively. Internal validation was estimated using 1,000 bootstrap resampling. The discrimination of the Osservatorio Epidemiologico sulla Sincope nel Lazio score was compared with the risk score in our cohort. Statistical analyses were performed using R version 4.1.1.

A total of 955 patients in 11 participating hospitals were included (mean age: 62 years; 421 [44.1%] female), in whom 112 (11.7%) patients had serious adverse events. Reflex, cardiac, orthostatic hypotension, and unexplained syncope occurred in 381 (39.9%), 313 (32.8%), 53 (5.5%), and 208 (21.8%) patients, respectively. Chinese Syncope Score (CSS) was created with 8 independent predictors of the outcomes: coronary artery disease, chronic kidney disease, cerebrovascular disease, first syncope occurring at >55 years of age, >4 episodes of syncope, predisposition to vasovagal syncope, ventricular arrhythmias on the electrocardiogram, and abnormal cardiac biomarkers, ranging from -2 to 6 (**Figure 1**). The risk score was stratified into 3 groups: low-risk (<2 points), intermediate-risk (2-3 points), and high-risk (>3 points), with a statistically significant difference based on the event-free survival curves (log-rank $P < 0.001$) (**Figure 1**). Both the Cox model and the risk score model discriminated well with C statistic values of 0.82 (95% CI: 0.80-0.87) and 0.83 (95% CI: 0.79-0.86) respectively. Discrimination of the CSS for predicting outcomes outperformed the Osservatorio Epidemiologico sulla Sincope nel Lazio score (C statistic: 0.73 [95% CI: 0.69-0.77]; $P < 0.001$). The calibration slopes were 1.04 for the Cox model and 0.89 for the risk score model, indicating good calibration. After bootstrap internal validation, the C statistics of the Cox model and risk score model were 0.81 (95% CI: 0.78-0.84)

FIGURE 1 Development of Chinese Syncope Score From a Multicenter Prospective Cohort



Calculations of the score and Kaplan-Meier survival curves of serious adverse events for syncope patients are presented.
ECG = electrocardiogram.

and 0.81 (95% CI: 0.78-0.85), with corresponding calibration slopes of 0.97 and 0.89.

To our knowledge, this is the first risk stratification score specifically developed for the Chinese population and the largest cohort study showing the adverse events of syncope patients in Asia. However, we could not compare the predictive accuracies of the CSS with the standard risk scores used earlier due to the unavailability of certain predictors in our dataset. Given that serious adverse events are rare, further investigations are warranted to ensure robust and consistent performance in larger patient cohorts and across different racial groups.

The CSS with relatively simple and well-defined predictors can be useful for physicians and easily incorporated into practice, and it would be suitable for Asian patients. After external validation, the CSS can be a valuable tool for efficient initial triage in diverse clinical settings.

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https://doi.org/10.1016/j.jacasi.2024.01.011

This work was supported by the National Natural Science Foundation of China (nos. 82170327 and 82370332 to Dr Tong Liu and no. 81270166 to Dr Wenling Liu) and the Tianjin Key Medical Discipline (Specialty) Construction Project (no. TJYXZDXK-029A). All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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