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Risk Stratification for Cardiac Complications in Patients Hospitalized for Community-Acquired Pneumonia

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Abstract

Objective: To derive and validate a clinical rule that stratifies the risk of cardiac complications in patients hospitalized for community-acquired pneumonia (CAP) and compare its performance to the pneumonia severity index (PSI) score.

Patients and Methods: Two cohorts of patients hospitalized for CAP were selected for the study. We used regression techniques in the derivation cohort (1343 patients enrolled in the Pneumonia Patient Outcomes Research Team study between October 1991 and March 1994) to generate a prediction rule that we validated in the validation cohort (608 patients enrolled in the Dissemination of Guidelines for Length of Stay study between February 1998 and March 1999). Discrimination and reclassification analyses compared its performance against the PSI score.

Results: A prediction model for cardiac complications in the derivation cohort included age, 3 preexisting conditions, 2 vital signs, and 7 common laboratory or radiographic parameters. Discrimination (C statistic, 0.81; 95% CI, 0.78-0.84) and calibration (Hosmer-Lemeshow goodness-of-fit test, χ^2=13.0; P=.11) were good. We derived a point score system from this model that when applied to the validation cohort also had good discrimination (C statistic, 0.78; 95% CI, 0.74-0.83) and calibration (Hosmer-Lemeshow, χ^2=9.0; P=.34). On the basis of this score, we defined 4 categories of incremental risk of cardiac complications. The incidence of cardiac complications across risk categories increased linearly (from lowest to highest) in both the derivation (3.0%, 17.8%, 35.2%, and 72.2%) and validation (5.0%, 8.2%, 28.3%, and 48.9%) cohorts (Cochran-Armitage linear trend test, P<.01). The new score outperformed the PSI score in predicting cardiac complications in the validation cohort (C statistic, 0.78 vs 0.74; P=.03; proportion of patients correctly reclassified by the new score, 44%).

Conclusion: We derived and validated a clinical rule that accurately stratifies the risk of cardiac complications in patients hospitalized for CAP.

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Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality worldwide.[1,2] Clinical cardiac complications occur in as many as 27% of patients hospitalized for CAP, are responsible for one-third of clinical failures of CAP treatment, and are the direct or underlying cause of death in one-quarter of CAP-associated fatalities.[3,4] The development of cardiac complications in patients with CAP increases short-term mortality by 60% to 200%.[3,5]

Given the importance of cardiac complications in the outcomes of patients with CAP, elucidating the mechanisms responsible for such events and preventing their occurrence are important goals.[4] In this context, a clinical tool that stratifies patients with CAP by their risk of development of cardiac complications would allow the identification of high-risk groups in which mechanistic studies could be executed most efficiently and targeted clinical interventions would be most beneficial. Because more than 50% of CAP-associated cardiac complications are recognized within 24 hours of presentation to the hospital,[3] this prediction rule must include elements that are readily available at the time of initial evaluation. Previous reports have suggested that the Pneumonia

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Severity Index (PSI) score, a validated and widely used tool for early stratification of the short-term risk of death in CAP patients,[6] can also predict the risk of CAP-associated cardiac events,[3,7] but whether a prediction rule designed specifically for cardiac complications improves risk stratification for cardiac events relative to the PSI score is unknown. Accordingly, our objective in the present study was to derive and validate a prediction rule for stratification of the short-term risk of cardiac complications in patients hospitalized for CAP and to compare its performance to the PSI score.

PATIENTS AND METHODS

Study Population

The derivation cohort consisted of 1343 inpatients from the Pneumonia Patient Outcomes Research Team (PORT) study,[8] a prospective observational study of patients with CAP presenting to 5 medical institutions in Pittsburgh, Pennsylvania; Boston, Massachusetts; and Halifax, Nova Scotia, Canada between October 1991 and March 1994. The validation cohort consisted of 608 patients from the Dissemination of Guidelines for Length of Stay (DGLoS) study,[9] a prospective study of patients with CAP admitted to 7 medical institutions in Pittsburgh between February 1998 and March 1999. We selected these cohorts because a recent systematic review of the literature determined that among studies of patients with CAP in whom cardiac complications were reported, these cohorts had the highest methodological standards.[10] Details of patient inclusion and exclusion criteria for each cohort are presented in Supplemental Table 1 (available online at http://www.mayoclinicproceedings.org).

The study protocols were approved by the institutional review boards of the participating institutions.

Baseline Data Collection, Follow-up, and Assessment of Outcomes

In both studies, data on baseline demographic characteristics, comorbid illnesses, physical examination findings, and results of radiographic and laboratory tests were prospectively collected. The incidence of clinical cardiac events within 30 days of presentation to the hospital was determined according to the operational definitions presented in Supplemental Table 2 (available online at http://www.mayoclinicproceedings.org). Cardiac complications were defined as (1) new or worsening heart failure, (2) new or worsening cardiac arrhythmias, or (3) acute myocardial infarction.

Statistical Analyses

Derivation of the Prediction Rule and Assessment of Internal Performance. These analyses were performed in the derivation cohort. Potential predictors of cardiac complications were selected on the basis of clinical and pathophysiologic considerations. Because treating physicians decided the level of clinical scrutiny and whether laboratory tests were clinically indicated on an individual patient basis (similar to the validation cohort),[8,9] random data absence could not be assumed, and multiple imputation techniques for managing missing data were not appropriate.[11] Instead, similar to the development of other widely validated clinical prediction rules,[12-14] missing values were assumed to fall within the clinically normal range. With the exception of age (no missing values), continuous variables were categorized as either 2- or 3-level categorical variables on the basis of common clinical criteria for normality and severity, inspection of empirical logit plots, and assessment of 5 operating characteristics (data density, sensitivity, specificity, total accuracy, and the Youden index).[15] All study patients were included for analyses. When variables were highly collinear,[16] we created an inclusive composite variable based on pathophysiologic and clinical considerations. We entered the pool of candidate predictors into a multivariate logistic regression model in which stepwise backward elimination was used to identify predictors of cardiac complications. The significance level for retaining variables in the model was α=.1. To assess model performance, we calculated the area under the receiver operating characteristic curve (C statistic). The calibration of the model was evaluated by the goodness-of-fit Hosmer-Lemeshow χ^2 statistic and by plotting expected vs observed rates of events across deciles of risk.[17] To evaluate the internal validity of the model, we generated 200 bootstrap samples and applied the stepwise variable selection procedure to each of them.[18] The degree of overfitting (optimism bias) of the model was estimated and used to calculate the optimism-