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CLINICAL RESEARCH

Risk Prediction in Patients With Heart Failure

A Systematic Review and Analysis

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ABSTRACT

OBJECTIVES This study sought to review the literature for risk prediction models in patients with heart failure and to identify the most consistently reported independent predictors of risk across models.

BACKGROUND Risk assessment provides information about patient prognosis, guides decision making about the type and intensity of care, and enables better understanding of provider performance.

METHODS MEDLINE and EMBASE were searched from January 1995 to March 2013, followed by hand searches of the retrieved reference lists. Studies were eligible if they reported at least 1 multivariable model for risk prediction of death, hospitalization, or both in patients with heart failure and reported model performance. We ranked reported individual risk predictors by their strength of association with the outcome and assessed the association of model performance with study characteristics.

RESULTS Sixty-four main models and 50 modifications from 48 studies met the inclusion criteria. Of the 64 main models, 43 models predicted death, 10 hospitalization, and 11 death or hospitalization. The discriminatory ability of the models for prediction of death appeared to be higher than that for prediction of death or hospitalization or prediction of hospitalization alone ($p = 0.0003$). A wide variation between studies in clinical settings, population characteristics, sample size, and variables used for model development was observed, but these features were not significantly associated with the discriminatory performance of the models. A few strong predictors emerged for prediction of death; the most consistently reported predictors were age, renal function, blood pressure, blood sodium level, left ventricular ejection fraction, sex, brain natriuretic peptide level, New York Heart Association functional class, diabetes, weight or body mass index, and exercise capacity.

CONCLUSIONS There are several clinically useful and well-validated death prediction models in patients with heart failure. Although the studies differed in many respects, the models largely included a few common markers of risk. (J Am Coll Cardiol HF 2014;2:440–6) © 2014 by the American College of Cardiology Foundation.

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Heart failure is a common and complex condition (1-3). Despite recent advances in diagnosis and management, average outcomes in patients with heart failure remain poor and highly variable (4). Risks among subgroups of patients with heart failure often vary several-fold and may change substantially over time. Hence, understanding expected risks and communicating anticipated future disease trajectories to patients and their families constitutes important aspects of patient-physician interactions in heart failure (5,6). More specifically, knowledge of future risks can help patients and clinicians make informed decisions about the initiation and intensity of treatment, such as device therapy, disease monitoring, or end-of-life care according to the individual patient's need and potential for benefit (7,8). Identification of low-risk patients, on the other hand, could help reduce patient anxiety and avoid costly interventions of questionable value (7,8).

However, how to best estimate risk in patients with heart failure is less clear (6,8,9). A substantial body of published data has shown that patients' and clinicians' intuitive judgments about future risk tend to be inaccurate and highly variable (10-14). This is partly due to our inability as individual people to simultaneously consider and process information about multiple factors. Furthermore, single predictors of risk are rarely sufficient for accurate estimation of risk for common conditions such as heart failure (15). A solution to this problem is to estimate risk from a combination of several predictors by using a statistical multivariable model (15-17).

There has recently been a rapid increase in the number of statistical models available. However, without a comprehensive overview, it remains unclear which, if any, should be applied in clinical care. Therefore, we reviewed contemporary published reports for multivariable statistical models for prediction of death, hospitalization, or both and assessed their utility for clinical decision making.

METHODS

We undertook this systematic review according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

SEARCH STRATEGY FOR IDENTIFICATION OF RELEVANT STUDIES. We searched MEDLINE and EMBASE from January 1995 to March 2013 for articles with terms or subject terms "re-admission" or "mortality" or "death" or "model" or "predict" and "heart failure." The search was limited to human studies; there was no language restriction. We also hand searched the reference lists of eligible studies as well as reviews relating to this subject for identification of additional relevant publications (the detailed search strategy is presented in Online Appendix 1).

REVIEW METHODS AND SELECTION CRITERIA. Two reviewers independently screened all titles and abstracts and made decisions regarding potential eligibility after full-text review. Discrepancies in judgment were resolved by a third reviewer. Studies were eligible if they reported multivariable models for prediction of risk of death, hospitalization, or death or hospitalization in people with heart failure; the derived model included at least 50 patients who experienced an event during the observation period, because studies with fewer cases are unlikely to be sufficiently robust for widespread clinical or administrative use; and they assessed model performance. We excluded studies that focused on single predictors of risk only, because these are prone to reporting overly optimistic findings due to a number of methodological limitations (15). We placed no restrictions on study setting, participant characteristics, or geographic regions.

DATA EXTRACTION. For each included study, the following information was extracted: study and patient characteristics, candidate variables considered for model derivation, final model variables and their strength of association with the outcome, analytical methods, and model discrimination, calibration, and validation, as reported by the authors. Discrimination is the ability of a statistical model to distinguish those subjects who experience the outcome from those who do not. It is usually reported using the C statistic. A C statistic of 1 indicates perfect discrimination, whereas a C statistic of 0.5 indicates discrimination no better than chance. We defined a C index of <0.6 as poor, 0.6 to 0.7 as modest, and >0.7 as good. Calibration is defined as how closely observed estimates of absolute risk agree with expected estimates from the risk prediction model and is best assessed graphically. We also recorded internal or external validation of the model, with the former being an assessment of model fit and the latter being an assessment of model generalizability. Internal validation is determined on the basis of the same data used to develop the model and is usually assessed via bootstrapping (18). External validation is assessed by how well the developed model performs on an independent sample (19).

DATA ANALYSIS. We explored whether a priori defined individual methodological characteristics were associated with the discrimination of the risk

ABBREVIATIONS AND ACRONYMS

BNP = brain natriuretic peptide

LMIC = low- and middle-income country

NT-proBNP = N-terminal pro-B-type brain natriuretic peptide

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