Critical Review Form
Clinical Prediction or Decision Rule

PGY-4

Auble TE, Hsieh M, Gardner W, Cooper GF, Stone RA, McCausland JB, Yealy DM. A prediction rule to identify low-risk patients with heart failure. Acad Emerg Med. 2005 Jun;12(6):514-21.

Objectives: **"to derive a clinical prediction rule based on data readily available in the ED to identify patients with heart failure who are at low risk of inpatient death or serious medical complications."**

Methods: **This retrospective cohort study was conducted using two statewide databases in Pennsylvania (the MediQual Atlas System and the Pennsylvania Health Care Cost Containment Council [PHC4]). Pennsylvania residents age 18 years or older, discharged in 1999 with a primary discharge diagnosis code consistent with heart failure were eligible for inclusion. Patients without a documented pulse rate, systolic blood pressure, and respiratory rate were excluded. Only initial hospital admissions in 1999 were included.**

The MediQual-Atlas System includes more than 300 key clinical findings for each patients, including demographic, historical, physical examination, laboratory, electrocardiographic, and imaging data. The Pennsylvania Department of Health Division of Vital Statistics was reviewed for mortality data for 1999 and the first 30 days of 2000.

Primary outcomes included inpatient death and a composite of inpatient death or serious complication during the index hospitalization. Serious complications included myocardial infarction, ventricular fibrillation, cardiogenic shock, cardiac arrest, or the need for any of the following: intubation, mechanical ventilation, cardiac compression, resuscitation, defibrillation, CABG, PCI, or IV thrombolytics. Secondary outcomes included a of all cause mortality within 30 days of admission and need for readmission within 30 days with a discharge diagnosis of heart failure.

A list of candidate variables readily available in the ED and found in previous studies to be prognostic of short-term or long-term adverse outcomes was considered in the construction of the clinical prediction rule. Statistical analysis was then used to derive the clinical decision rule, which was not validated on a separate sample.

Out of 47107 hospital admissions for heart failure, 43531 (92.4%) had the required ED vital signs documented. Of these, 33,533 represented the initial hospitalization for the involved patients. 83.1% of patients were older than 65, 56.4% were female, and 80.2% were of white race. There were 1498 deaths during hospitalization (4.5%) and 2269 patients who survived to discharge but had a serious complication (6.8%).

There were 2633 deaths (7.9%) and 2368 patients readmissions at least once within 30 days of the index admission (7.1%).

Guide		Comments
I.	***Is this a newly derived instrument* (Level IV)?**	
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	Yes. The authors specifically report than "We used the entire cohort for derivation rather than splitting it into development and validation samples." (p. 517). Bootstrap resampling and K-fold cross-validation were used to estimate the precision and prediction errors for the outcomes.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	
1a	Were all important predictors included in the derivation process?	Mostly yes. The authors chose a vast array of prognostic factors to include in their derivation, including demographic and historical factors, vital signs, laboratory values, electrocardiographic variables, and radiographic findings. Age, oddly, was not included in the derivation, nor was ejection fraction in those patients with a recent ECHO.
1b	Were all important predictors present in significant proportion of the study population?	Yes for some variables, uncertain for many others. For those historical factors for which the authors provide a percentage of patients positive for the factor (heart failure, MI, angina, lung disease, renal disease) there were a significant number of patients with these historical factors. Additionally, a significant proportion of patients were found to have radiographic abnormalities (pleural effusion, cardiomegaly, and pulmonary congestion) and ECG abnormalities (a-fib/flutter, MI, myocardial ischemia). Many of the predictors are continuous variables, but the authors do not provide the overall range or interquartile ranges for these variables.
1c	Does the rule make clinical sense?	Uncertain. The authors devised a classification tree, and while they refer to this as a "clinical decision rule," they do not provide sufficient details on how the rule is used to make it clinically feasible to do so. They provide no actual details on what final factors were included in the rule or how these factors were used to determine which patients were low risk.
2	Did validation include prospective studies on several different	No validation was performed prospectively. Bootstrapping and other statistical techniques

	populations from that used to derive it (II) or was it restricted to a single population (III)?	were used to predict error.
3	*How well did the validation study meet the following criteria?*	
3a	Did the patients represent a wide spectrum of severity of disease?	No. This study included only patients admitted and later discharged from the hospital with heart failure. This did not include patients discharged directly from the ER, who would likely be on the low end of risk. Beyond this, the authors provide very little information regarding the spectrum of disease seen (i.e. range of ejection fractions, degree of pulmonary edema and peripheral edema, etc.)
3b	Was there a blinded assessment of the gold standard?	Uncertain. While there is no specific gold standard, several fairly objective outcomes were used, including death, mechanical ventilation, and ventricular fibrillation. Other outcomes were more subjective, such as myocardial infarction. All outcomes aside from death were based on ICD-9 codes at discharge. The authors do not mention any blinding of those assessing these ICD-9 codes.
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Uncertain. The authors do not mention any blinding of investigators to the outcomes, and hence they may have been aware of outcomes when assessing the predictor variables. Most of the predictor variables were objective (vital signs, lab measurements) but other such as medical history, CXR findings, and ECG findings may be somewhat subjective. The authors provide no information regarding the methods of interpreting these variables.
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	N/A. There was no gold standard performed. All outcomes were based on ICD-9 codes.
4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	The rule classified 5758 (17.2%) patients as low risk. Among these, there were 19 inpatient deaths (0.3%) and 59 survivors with an inpatient serious complication (1.0%). There were 114 patients with death within 30 days of admission (2.0%) and 290 were readmitted at least once for heart failure within 30 days of the index admission (5.0%).
III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	
1	How well did the study guard	Not well. The authors make no mention of

	against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	blinding those recording and interpreting prediction variables or those assessing outcomes. There is reportedly no loss to follow-up, as the authors make the assumption that all outcomes would be captured by the PHC4 and Atlas systems. The validity of such an assumption is uncertain.
2	What was the impact on clinician behavior and patient-important outcomes?	No impact analysis was conducted. The rule was able to identify a significant number of patients who would classified as low risk (17.2%). If validated and shown to be safe, such a rule could in theory result in a significant reduction in admission rates.

Limitations:

1. **Bootstrapping was used to validate the rule, rather than independent validation in a new subset of patients. This is therefore a level 4 rule and cannot be used until it is validated in multiple environments.**

2. **The CRD derived is quite complicated, requiring multiple steps to obtain a final risk, and is not provided in full in the body of the paper. It would likely be too cumbersome to be of clinical utility.**

3. **Among patients considered to be low risk, 0.3% died during the index hospitalization and 2% died within 30 days. Further evaluation of baseline risk and acceptable risk will be needed to determine if such patients are truly "low risk."**

4. **The authors evaluate risk of outcomes in a cohort of patients admitted to the hospital. It is uncertain if the risk of adverse events was altered by the admission itself (and subsequent monitoring and treatment). It may be that such patients would be at higher risk if they were discharged from the ED.**

Bottom Line:

This retrospective cohort study evaluated patients admitted for acute heart failure in an attempt to derive a clinical decision rule to identify patients at low risk of adverse events. They were able to devise a rule that identified 17.2% of their cohort as low-risk. In this group, 0.3% died while inpatients and 2% died within 30 days, with 5% being readmitted within 30 days. The rule has not been validated and no impact analysis has been performed. The rule itself sounds quite cumbersome and was not actually provided in the body of the paper.