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ACUTE Heart Failure Risk Stratification: A Step Closer to the Holy Grail?

Sean P. Collins, MD, MSc[1] and **Peter S. Pang, MD, MSc**[2]

[1]Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN

[2]Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, IN

Over 80% of all emergency department (ED) visits result in discharge. Conversely, over 80% of ED patients with AHF are admitted to the hospital. Disappointingly, this practice persists despite 20 years of effort, with little reason to believe it will change.[1] While some patients clearly benefit from hospitalization, up to 50% of ED patients with AHF may be discharged or placed in observation.[2, 3] Importantly, nearly half of all patients hospitalized with AHF present with lower risk features, such as a blood pressure > 140mmHg and a BNP < 1000 pg/mL, supporting the idea of a lower risk cohort embedded within the overall AHF population.[4] However, this cohort has many associated comorbidities. More importantly, a significant proportion is likely to experience an adverse event at rates perceived by most emergency physicians as too high for ED discharge.[5]

Many other ED-based cardiovascular disease processes (evaluations for acute coronary syndrome or pulmonary embolism) have evolved from high rates of admission to timely and safe ED discharge. Decision making in AHF has not experienced a similar evolution. There are several possible explanations for this lack of progress and we highlight several. First, ED providers may believe hospitalization imparts a protective effect and changes the trajectory of patient's outcomes. While decongestion is a cornerstone of hospital management, there is no AHF therapy that definitively improves outcomes.[6] Second, lack of early and aggressive ED-based therapy in an effort to improve symptoms and facilitate ED discharge is all too common. While these two challenges could be overcome, the third and greatest challenge remains: without an externally validated tool to identify low-risk AHF patients for safe, early discharge, risk-averse emergency physicians will default towards hospital admission. No doubt, risk-stratification remains an unmet need.

There is good news however. Greater efforts toward ED AHF risk-stratification have yielded instruments with adequate, even excellent, discriminatory statistics. Yet such risk-rules either suffer from limitations or external factors limiting their applicability, including retrospective cohort methodology, lack of external validation, different national healthcare systems, and decision rule complexity. (Table).

While there are exceptions, one notable limitation is their inclusion of high-risk features that most emergency physicians would consider automatic exclusions for discharge. Specific

Corresponding Author: Sean P. Collins, MD, MSc, 1313 21st Ave South, Nashville, TN 37232, Sean.collins@vumc.org, 615-875-6151 (p).

examples include significantly worse acute kidney injury (AKI) or high troponin values. Importantly, the inability to determine the additive value of the risk score when combined with provider-estimated risk is worth highlighting. Physicians commonly believe in their own ability to estimate risk; yet in AHF, we appear to send patients home who are more likely to die than those we admit,[12] admit patients who have an uneventful and brief hospital stay, and remain surprised by the proportion (4%) who experience death within 30-days.[13] This also makes one consider the competing risk of death and non-fatal re-hospitalization. Which risk is more concerning? Should we consider the event with the higher financial penalty? Both are important, especially to patients. However, stratifying the risk for death is paramount.

In this edition of Circulation, Lee and colleagues externally tested their 7-day (EHMRG7 – Emergency Heart Failure Mortality Risk Grade) and 30-day (EHMRG30) risk score in nearly 2000 patients at 9 hospitals in Ontario, Canada.[14] Compared to most prior risk-stratification studies, the authors externally tested their original rule in a prospective manner, in a separate cohort of patients, simultaneously determined physician estimated risk, and performed comprehensive follow-up. This step is critical prior to an implementation study. Importantly, a waiver of informed consent facilitated enrollment along the entire spectrum of disease severity. Their patients were older (median 81 years), with 71% having a prior diagnosis of HF, and a fair proportion of CV and non-CV comorbidities. Of these patients, 21% were discharged from the ED. Those patients discharged home had <1.5% 7-day and 3.3% 30-day mortality. Within 7 days, 39 patients died (2%) and by day 30 this rose to 138 patients (7%). Of the 138 deaths, only 17 occurred outside the hospital. They divided patients into 5 pre-specified risk categories: very-low, low, intermediate, high, and very high. Patients in the very-low or low-risk (518 patients) categories had 7-day and 30-day mortality rates of 0%. The discrimination for physician estimated risk (AUC=0.71) was improved (AUC=0.82) with use of the EHMRG7 model (AUC=0.81). The EHMRG30 had slightly lower (0.77) discrimination when compared to EHMRG7. Another important key finding is the over-estimation of 7-day and 30-day mortality at the low-end of the risk spectrum by providers, and an underestimation of mortality at the higher end.

From the ED standpoint, 0% mortality at 7 and 30 days in the low risk group is very reassuring. Emergency physicians' overestimation of risk in these same patients highlights the need for an objective score. Still, it would be good to know what element of the risk-score drove categorization. Dichotomizing certain variables – such as EMS transport (at times inappropriately utilized in the US) and troponin (how positive?) – may sway the risk rule. Using an online EHMRG calculator, it is possible to categorize patients with either a SBP of 80mmHg, a very high troponin value, or significantly worse acute kidney injury into the low-risk group. This brings the challenge of real-world applicability into the crosshairs; for the decision rule to be used, it must account for patients who clearly need admission, but are categorized by the risk-score as low-risk. Arguably, this is unfair to the decision rule and discounts the rigor by which this rule was developed. Further, it renders clinical judgment obsolete. Nevertheless, it highlights the need for an implementation study. The absence of high-risk features in EMHRG suggests a lower-risk patient, however, they still may not be eligible for discharge because of other complicating and competing conditions.

This study advances our understanding of the EHMRG rule, and risk-stratification in general, but there are several limitations to consider. Nearly 30% of patients have no prior history of HF. Although management of de novo HF varies country by country, in the US, such patients generally warrant admission. The need for decongestion, identification and management of precipitants, as well as investigating underlying cardiac structure and function is challenging to accomplish outside of the hospital setting. Similarly, how well does the model discriminate when high-risk patients are excluded? A risk rule for discharge has less utility in patients with hypotension, who require non-invasive or invasive ventilation, have very high troponin values or severe acute kidney injury. Once all the appropriate reasons to admit are taken out, how then do we decide what to do? Data collection was not standardized, and this can introduce inconsistency and inaccuracies. The authors discuss the use of net reclassification index to suggest how the EHMRG rule could impact physician decision making. However, this may not be a completely accurate picture of the rule's impact. While there is a clear need to identify lower-risk patients safe for ED discharge, provider decision making accounts for the possible success of outpatient management given the severity of both AHF and non-AHF symptoms. Finally, the standard work-up in the participating EDs did not routinely include the use of natriuretic peptides or an electrocardiogram. Natriuretic peptides have been found in other risk models to be an important variable in the risk-stratification model.[7, 10]

Are we any closer to the holy grail of safe ED discharge based on an AHF risk rule? The EHMRG rule uses readily available data to stratify patients into low and very-low risk categories. It has been derived and externally tested in large cohorts of patients. The next logical step is to incorporate natriuretic peptides into the rule and test the additive value of this rule alongside provider risk estimation in a large randomized trial that includes a population of patients across the spectrum of disease severity throughout the US and Canada.

However, establishing a risk-rule is just one component needed to change the current ED approach to disposition decision making.[15] Early, aggressive treatment is also necessary so that patients experience adequate symptom relief. Waiting to provide treatment until after the work-up is complete, or not providing sufficient treatment introduces unnecessary delays, fails to provide sufficient symptom relief and could prevent ED discharge. Once appropriately treated and risk-stratified, a reliable mechanism for early outpatient follow-up is mandatory. Some ED patients with AHF will have an established patient-provider relationship where outpatient follow-up is easily facilitated. However, rapid outpatient access for all patients regardless of the time of ED discharge and previous provider relationship is crucial for success.

Over the next decade there are great opportunities to increase the proportion of ED patients with AHF who can be safely discharged home. While such needed progress is unlikely to match the state of disposition decision making in other cardiovascular processes in the ED such as chest pain, studies such as ACUTE are a necessary step in the right direction. Other AHF rules require similar external testing and implementation studies to determine their optimal role in the ED. Such continued advances will help drive further improvements in

early treatment and local support for rapid outpatient follow-up – necessary items to safely discharge a larger proportion of patients with AHF.

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Table.

Risk-Instruments to Identify Low Risk for ED Discharge

	Year	Sample size	Country	Variables	Risk stratification goal	External Validation	Clinical Validation
Stiell et.al.[7] Ottawa Heart Failure Risk Scale	2017	1100	Canada	- History of stroke or TIA - History of intubation for respiratory distress - Heart rate on ED arrival >=110 - Room Air SaO2 <90% on EMS or ED arrival - ECG has acute ischemic changes - Urea >=12 - Serum CO2 >=35 - Troponin I or T elevated to MI level - NTproBNP >=5000 - During Walk test, SaO2 <90% on room air or usual O2, or HR >= 100 during 3-minute walk test, or too ill to walk	30-day serious adverse events	Yes	Maybe: clinicians told not to solely base their decision on OHFRS
Miro et.al.[8] MEESI	2018	4711	Spain	- Barthel index at admission - Systolic blood pressure - Age - NTproBNP - Potassium - Troponin - NYHA at admission - Respiratory rate - Low output symptoms? - Oxygen saturation - Episode associated with ACS? - Hypertrophy on ECG? - Creatinine	30-day mortality	Yes	No
Lee et.al. EHMRG[9]	2018	1983	Canada	- Age - Arrival by ambulance - Systolic blood pressure (triage) - Heart rate (triage) - Oxygen saturation (triage) - Potassium - Creatinine - Troponin - Active cancer - Metolazone use prior to ED arrival - ST depression on 12 lead (30-day model)	7 and 30-day mortality	Yes	No
Collins et.al. [10] STRATIFY	2015	1033	US	-Age -BMI -BNP -Diastolic blood pressure -BUN -Sodium -Respiratory Rate -Oxygen Saturation -Troponin -Dialysis -On supplemental oxygen -On outpatient ACEI -QRS duration	5 and 30-day hierarchical adverse events	No	No
Auble et.al.[11] Acute Heart Failure Index	2008	8384	US	- Sex - History of (h/o) MI - h/o angina - h/o PTCA	Death or serious medical complication before discharge.	Yes	No

	Year	Sample size	Country	Variables	Risk stratification goal	External Validation	Clinical Validation
				- h/o diabetes - h/o lung disease - Heart rate - Respiratory Rate - Systolic Blood Pressure - Temperature - Sodium - Potassium - BUN - Creatinine - Glucose - WBC count - Arterial pH - ECG findings: MI - ECG findings: Ischemia - CXR: pulmonary congestion - CXR: pleural effusion	Secondary: Inpatient death alone and 30-day mortality alone		