REVIEW

Identification of patients with acute heart failure safe for emergency department discharge

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Abstract: Objectives – The emergency department (ED) is the starting point of care for the vast majority of patients hospitalized with acute heart failure (AHF). However, the evidence base to guide dispositions decisions and identify patients for early, safe discharge is relatively weak. As a result, the majority of patients are admitted. However, because clinicians are faced with the daily challenge of risk-stratifying patients to help determine who potentially could be sent home, this remains an area of intense investigation. In this review, we outline an expert consensus on how to risk-stratify ED patients with AHF. **Methodology –** Expert consensus literature review. **Results –** The evidence to support firm conclusions regarding risk-stratification to identify a low risk-cohort safe for ED discharge is lacking. Several risk scores have been developed, though all have limitations, suggesting they should not be routinely used in clinical practice. However, several of these scores are currently undergoing external validation. Patients with elevated blood pressure, preserved renal function and a normal cardiac troponin during their ED work-up are lower risk. In combination with good response to ED therapy, close outpatient follow up, and good self-care skills, these patients represent candidates for early, safe ED discharge. **Conclusions –** Most ED patients with AHF are admitted, however, a sizable proportion may be safely discharged. Although further work is needed, identification of lower risk patients is currently possible with existing risk markers, such as blood pressure, renal function, and troponin.

Key words: acute heart failure, emergency department, discharge, risk stratification

Rezumat: Obiective – Departamentul de urgență (ED) este punctul de la care pornește tratamentul pentru marea majoritate a pacienților spitalizați cu diagnosticul de insuficiență cardiacă acută (AHF). Cu toate acestea, ghidurile actuale privind recomandările de internare sau nu a pacienților cu insuficiență cardiacă în camera de gardă sunt destul de vagi. Prin urmare, majoritatea pacienților sunt spitalizați. Cu toate acestea, medicii se confruntă zilnic cu provocarea de a reuși o stratificare a riscului pacienților aflați în camera de gardă și acestă provocare. În această lucrare, vom prezenta un consens al experților cu privire la stratificarea riscului pacientilor din ED diagnosticați cu AHF. **Metodologie –** Consensul experților din domeniu asupra literaturii de specialitate. **Rezultate obținute –** Dovezile pentru a susține concluzii ferme în ceea ce privește riscul de stratificare pentru pacienții cu risc scăzut în departamentul de urgență sunt puține. Au fost elaborate mai multe scoruri de risc, ceea ce sugerează că acestea nu ar trebui să fie o rutină în a fi folosite în practica clinică. Cu toate acestea, mai multe dintre aceste scoruri sunt în curs de validare. Pacienții cu hipertensiune arterială, funcția renală prezervată și o valoare a troponinei cardiace normală în timpul ED reprezintă pacienți cu risc mic. Dacă răspund bine la terapia din ED, sunt urmăriți frecvent ambulator și prezintă bune abilități de auto-îngrijire, acești pacienți sunt candidați pentru externare precoce din ED în condiții de siguranță. **Concluzii –** Cei mai multi pacienți din ED cu AHF sunt internați, și cu toate acestea, o proporție considerabilă din acești pacienți pot fi externați precoce în condiții de siguranță. Cu toate că sunt necesare studii viitoare, identificarea pacienților cu risc scăzut este posibilă în condițiile existenței markerilor de risc, cum ar fi: tensiunea arterială, funcția renală și troponina.

Cuvinte cheie: insuficiență cardiacă acută, departamentul de urgență, externare, stratificarea riscului

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INTRODUCTION

Emergency department (ED) physicians diagnose and initially manage the vast majority of patients hospitalized with acute heart failure (AHF). Nearly 75% of ED visits for AHF ultimately lead to hospitalization; this high proportion of ED visits with resultant inpatient admission has not changed over the last decade, either in Europe or the US[1,2]. Hospital length of stay is 4-5 days in the US and 5-10 days or longer in the rest of the world[3]. The high financial burden and morbidity associated with hospitalization and subsequent rehospitalizations have led to increased scrutiny concerning AHF management and financial penalties for hospitals with excessive readmissions[2,4-9]. Attempts to reduce hospitalizations and readmissions, as well as improve outcomes have resulted in a myriad of management strategies, including development of novel therapeutics. While no single strategy of care has been proven to work in all clinical settings, HF readmissions are slowly decreasing[10]. From a therapeutic standpoint, clinical trials in chronic HF have demonstrated morbidity and mortality improvements[11-16]. However, similar benefits have yet to be achieved in AHF clinical trials[17-19].

The burden of inpatient admissions and the failure of acute therapy to definitively alter outcomes has led to renewed interest in risk-stratification; namely, determining who can be discharged home either directly from the ED or after a brief period of observation. As relatively few inpatients receive intensive acute care, mechanical ventilation, circulatory support, or undergo invasive diagnostic or therapeutic interventions, inpatient admissions might be avoided in a sizable proportion of patients[20,21]. However, it is unclear at present which patients can be safely discharged home.

RISK STRATIFICATION DURING EMERGENCY DEPARTMENT EVALUATION

Risk stratification has typically focused on the prediction of acute inpatient mortality, rather than re-hospitalization. Further, the majority of studies focus on identifying high-risk, rather than low-risk, and have been limited by a retrospective design in hospitalized patients. Identification of patients at low risk is the critical decision threshold for consideration of ED discharge, as most patients are currently admitted. Unfortunately, ED patients have traditionally not been enrolled in risk-stratification studies; most investigations have been hospital based and patients discharged from the ED are rarely included. Despite these limitations, low blood pressure, renal dysfunction, low serum sodium, and elevated cardiac biomarkers (troponin [Tn] or natriuretic peptides [NP]) have been repeatedly shown to be associated with increased morbidity and mortality[22].

As more studies attempt to delineate high-risk versus low-risk cohorts using simple, rapidly available data points, such as systolic blood pressure (SBP), heart rate, and oxygen requirement have proven to be important markers for rapid assessment and disposition. In the EHMRG 7-day mortality risk score, mortality risk increased with higher triage heart rate (OR, 1.15 [CI, 1.02 to 1.30]), lower triage SBP (OR, 1.52 [CI, 1.31 to 1.77] per 20 mm Hg), and lower initial oxygen saturation (OR, 1.16 [CI, 1.01 to 1.33] per 5%)[23]. However, this study was limited by retrospective patient identification, exclusion of early readmission for AHF as an outcome, and a practice environment not reflective of the United States. Stiell and colleagues found both heart rate >110 beats/min and oxygen saturation less than 90% at ED arrival were independent predictors of serious adverse events (SAEs)[24]. In AHF patients who are ultimately admitted, those with SBP of less than 120 mmHg had threefold higher inpatient mortality than those with SBP greater than 140 mmHg (7.2% vs 2.5%, p <0.001)[25]. In the HF patient who presents in acute distress, a lower initial SBP may reflect reduced left ventricular contractile reserve while a higher initial heart rate suggests the need for increased chronotropy to maintain cardiac output and increased sympathoadrenergic response. A lower initial oxygen saturation demonstrates increased pulmonary congestion and underlying respiratory compromise and therefore places the patient at increased risk for mortality[23]. Similar to the Lee et al. study, the practice environment in this Canadian study is markedly different than the US, as evidenced by the majority of ED patients being discharged.

Auble and colleagues derived a prediction rule using administrative data from over 33,000 patients. Their goal was to utilize variables readily available during an ED evaluation to identify a patient cohort whose risk of death or serious inpatient complications was less than 2%[26]. Secondary outcomes included death from any cause within 30 days of the index ED admission and the first hospital readmission during this interval with a primary discharge diagnosis of heart failure. Their complex model used 21 predictor variables to identify 17% of patients as low-risk. They subsequently externally tested their 21-variable mo-

del in an administrative cohort of over 8300 patients 27 and identified 19.2% of patients as being low risk (<2% inpatient death or complications and <1% inpatient death). Within this group of low-risk patients, 2.9% died within 30 days. Their model is robust, but is based on administrative data and does not account for other important events during the 30-day outpatient period such as ACS, unstable arrhythmias or readmission.

STRATIFY was a recent multi-center, prospective cohort study that enrolled 1,033 ED patients with AHF, including 7.7% that were discharged from the ED, to evaluate the incidence of SAEs within 30 days of ED evaluation (ACS, coronary revascularization, emergent dialysis, intubation, mechanical cardiac support, CPR, and death)[28]. The study assessed readily identifiable ED variables to select a patient cohort who may be eligible for ED discharge. The resultant decision tool was highly sensitive for 30-day mortality and SAE. Those patients with less than 3% and 5% risk for 30-day events were detected with 100% and 95% sensitivity, respectively (Table 1). Importantly, there were no deaths in the group at less than 3% risk and only one in the group with less than 5% risk of events. The rule did not consider HF readmission as an endpoint.

Organ Injury as a Marker of Risk: Do all patients with stable, elevated Troponin need admission?

Evidence of ongoing ischemia or myocardial injury, as demonstrated by ECG changes and elevated troponin, continues to be strongly associated with increased inpatient and post-discharge mortality and increased readmission rates. The presence of ST-depression on the ECG provided improved recognition of those patients with AHF at higher risk of 30-day mortality[29]. Peacock et al. illustrated that AHF patients with elevated cTn (and SCr <2.0) had higher in-hospital mortality compared to those without elevated cTn. However, this study utilized first generation troponin assays; many patients who may have elevated troponin levels as measured by the contemporary assays may have been in the "normal troponin" group in this study. Diercks et.al. showed a small OU cohort with a SBP >160 mmHg and a normal cTn suffered no 30-day adverse events (death, readmission, myocardial infarction, or arrhythmias)[30]. The recently derived risk prediction tools outlined above have likewise identified an elevated cTn level as an independent predictor of both SAE and mortality[23,24,28]. Despite these findings identifying a higher-risk cohort, patients with minimally elevated cTn levels may still be candidates for observation management, especially if serial troponin measurements are followed to exclude acute coronary syndrome (ACS). Troponin elevation in patients with AHF is not uncommon, though the majority are not due to ACS[31]. Many patients have low cTn levels above the 99%ile cutoff that may not confer an elevated risk of cardiac events when compared to those with ACS or significant cTn elevation. In the STRATIFY study cTn elevation did not confer increased risk until it was above 0.13 ng/ml (99%ile cutoff <0.04 ng/ml). Further study is needed however before recommended use in clinical practice. With the anticipated introduction of high-sensitive cTn assays in the US, identifying a level of cTn elevation that differentiates low-risk from non-low-risk patients with AHF is critical. Pang et.al. recently found when hsTnT was not above the 99th%ile patients were at very low risk for 180 day CV mortality[32]. In the past, absence of high risk features did not necessarily translate to sufficiently low risk for discharge. However, a pilot trial to prospectively test both the utility of a nondetectable or very low hsTnT release is ongoing. Additionally, this trial will prospectively collect STRATIFY variables to allow for external validation of that decision rule[33].

Natriuretic Peptides

The natriuretic peptides, B-type natriuretic peptide (BNP) and its N-terminal precursor fragment (NT-proBNP,) are the most established AHF biomarkers for evaluating undifferentiated dyspnea and assessing for worsening HF[34,35]. Patients with a BNP level less than 100 pg/mL are unlikely to have AHF and multiple studies have shown that rising BNP and NT-proBNP

Table 1. Test characteristics in low-risk patients in the STRATIFY decision tool

Cut point (%)	TN	FP	FN	TP	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
3	14	893	0	126	1.00 (0.97, 1.00)	0.02 (0.01, 0.03)	0.12 (0.10, 0.15)	1.00 (0.78, 1.00)
5	128	779	6	120	0.95 (0.90, 0.98)	0.14 (0.12, 0.17)	0.13 (0.11, 0.16)	0.96 (0.91, 0.98)
10	475	432	36	90	0.71 (0.63, 0.79)	0.52 (0.49, 0.56)	0.17 (0.14, 0.21)	0.93 (0.90, 0.95)

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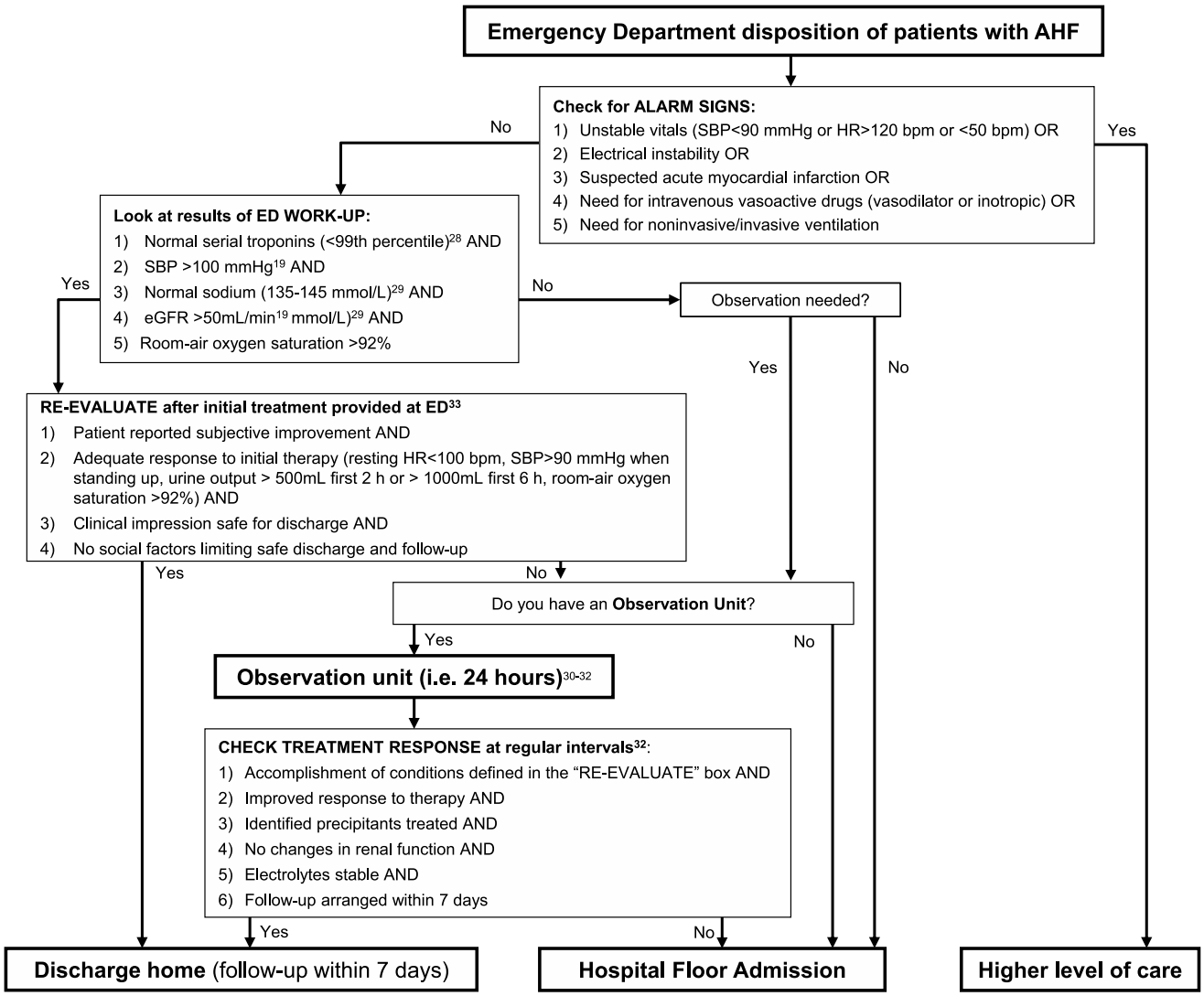

Figure 1. Consensus algorithm identifying patients who may be discharged directly from the ED or after a brief period of observation.

levels are associated with increased disease severity as well as an increased risk for mortality in AHF[36-38]. Nonetheless, there remains no absolute cutoff for these markers in regards to evaluating safe ED discharge. Clinical trials have shown limited effect of routine BNP measurement in predicting patient outcomes, and following BNP levels to gauge response to therapy or suitability for "safe" discharge have revealed mixed results[39-42].

International Consensus

A recent consensus paper from an international group of physicians and nurses, comprised primarily of ED caregivers, has further highlighted this issue of identifying ED patents for early, safe discharge from the ED[43]. A significant knowledge gap was highlighted by the group: what are the current event rates for discharged ED patients with AHF, and what is acceptable? Despite an extensive literature search, no universal evidence based consensus recommendation was provided, highlighting the need for continued work in this area. However, the group did propose event thresholds to advance research in this area, and suggested stratifying event rates by the ability of the ED to provide observation care (<48 hours). In addition, a consensus algorithm was proposed (Figure 1). While not intended for immediate clinical use, the consensus algorithm was put forth for local institutions to consider for both quality improvement and research efforts until it can be prospectively tested.

WHAT OTHER FACTORS SHOULD BE CONSIDERED IN PATIENTS WHO CAN BE DISCHARGED?

While the formal ED clinical evaluation is a crucial component of identifying patients safe for discharge, evaluating the patient's ability to provide self-care as well as the availability and degree of caregiver support may be equally important[44]. This includes socioeconomic considerations, such as the ability to afford medications, as well as transportation to follow-up appointments. Patients who have poor disease insight or lack access to medications or close outpatient follow-up may be poor candidates for direct ED discharge[45]. They may require an extended time period of ED-based observation or inpatient admission while an outpatient plan of care is established. While this may introduce additional cost, the potential subsequent healthcare costs and quality of life should also be considered. Finally, an improvement in symptoms due to ED-based AHF therapy is equally important. Often patients who have a low-risk ED-based evaluation and good social support may still require admission because of the inability of ED-delivered therapy to improve symptoms sufficiently to allow ED discharge.

CONCLUSION

Summarizing the available data to date suggests patients with elevated blood pressure, normal cTn, serum sodium and renal function, as well as an adequate response to ED therapy and good outpatient support are candidates for ED discharge. However, with external testing of the two prospectively derived risk-stratification studies this may change subsequent recommendations. The availability of a HF score utilizing readily available ED data would significantly impact current disposition strategies. The STRATIFY rule is currently being externally tested in a prospective multi-center study with anticipated completion of patient enrollment in 2018[33]. Until the results of these studies are available we suggest using a focused ED-based evaluation to safely transition a subset of ED patients with AHF away from hospitalization.

Teaching points:

1. The ED is the focal point for the initial diagnosis and management of the majority of patients who are admitted to the hospital with AHF.
2. The identification of low risk patients in ED remains challenging and is more complex than many other disease processes that present to the ED.
3. The vast majority of AHF studies have focused on identification of high-risk features in the ED patients.
4. Just because a patient does not have high-risk features does not mean they are low-risk and able to be discharged from the ED.
5. Clinical variables have been identified that may delineate low-risk from high-risk patients (SBP, cTn, BNP, renal function, serum sodium) but the absence of prospective validation limits their implementation in clinical practice.
6. In addition to clinical variables, two important components of ED evaluation include response to initial therapy and the patient's self-care ability, which may be influenced by socio-economic and caregiver factors.

Conflicts of interest:

Collins: Research Support: NIH/NHLBI, PCORI, Cardiorentis, Novartis, Trinity; Consulting: Trevena, Novartis, Siemens

Chioncel: Research Support: Servier, Vifor, Novartis, Philips

Fermann: Research Support: PCORI, Novartis, Siemens, Nanodetection, Cardiorentis, Trevena, Pfizer, Portola. Consulting: Janssen. Speakers Bureau-Janssen

Levy: Research Support: NIH/NIMHD, NIH/NHLBI, PCORI, Cardiorentis; Consulting: Cardiorentis, Trevena, Novartis, Siemens; Roche Diagnostics, ZS Pharma

Storrow: Current or Recent Research Support: Centers for Medicaid and Medicare Services (CMS), NIH / NHLBI, National Center for Advancing Translational Sciences/NIH, Beckman Coulter, PCORI. Current or Recent Consultant: Trevena, Beckman Coulter, Siemens, MCM Education

Pang: Consultant for: BMS, Medtronic, the Medicines Company, Novartis, Trevena, scPharmaceuticals, Cardioxyl, Roche Diagnostics, Relypsa; Research Support: Roche, Novartis, PCORI, IUSM

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