REVIEW

Hospitalized Patients with Acute Decompensated Heart Failure: Recognition, Risk Stratification, and Treatment Review

Alpesh Amin, MD, MBA, FACP

University of California Irvine, Irvine, CA.

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Acute decompensated heart failure (ADHF) has emerged as a major healthcare problem. It causes approximately 3% of all hospitalizations in the United States, with the direct medical cost of these hospitalizations estimated at $18.8 billion per year. Early recognition, risk stratification, and evidence-based treatment are crucial in reducing the morbidity, mortality, and costs associated with this disorder. Classic signs and symptoms of ADHF, such as rales, dyspnea, and peripheral edema, may be absent at hospital presentation and, even when present, are not specific to this disorder. As a result, serum B–type natriuretic peptide level is now used to rapidly and accurately detect ADHF. Multivariate analyses have identified renal dysfunction, hypotension, advanced age, hyponatremia, and comorbidities as significant and independent mortality risk factors. Based on these factors, mortality risk can be stratified from very low to very high using published algorithms that have been validated in independent populations. Evidence-based guidelines for the treatment of ADHF are available from both the European Society of Cardiology and the Heart Failure Society of America. In general, an intravenous loop diuretic, either alone or in combination with a vasodilator, is recommended as initial therapy in patients with volume overload, depending on the patient's clinical status. Use of inotropic agents should be limited to the small subset of patients with low-output syndrome and significant hypotension. In any event, frequent monitoring of clinical response is essential, with subsequent therapy determined by this response. Finally, focused patient education during hospitalization may help reduce readmissions for ADHF. ***Journal of Hospital Medicine*** **2008;3(Suppl 6):S16–S24.** © *2008 Society of Hospital Medicine.*

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Currently, acute decompensated heart failure (ADHF) accounts for 3% of all hospitalizations in the United States and is the second most common indication for hospitalization in individuals $\geq$65 years of age.[1] These hospitalizations are costly and frequently have limited sustained benefits. The total direct medical cost attributable to ADHF hospitalization in the United States is estimated to be $18.8 billion annually.[2] Furthermore, 50% of all patients hospitalized for ADHF are readmitted within 6 months of discharge.[3] Clearly, the hospital management of these patients requires reevaluation.

The purpose of this article is to review the recognition, risk stratification, and treatment of ADHF and to discuss the role hospitalists can play in improving this treatment.

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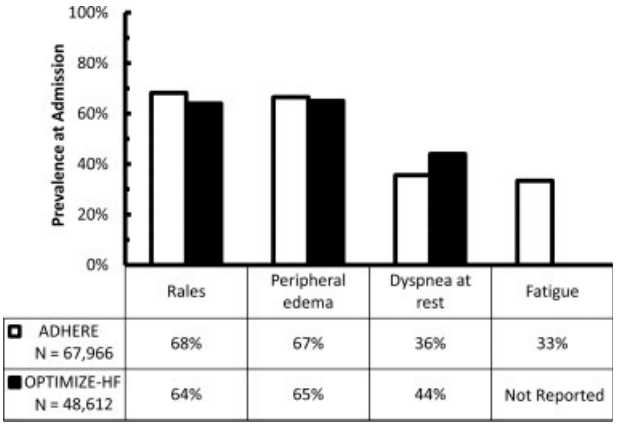
RECOGNITION OF ADHF

The American College of Cardiology/American Heart Association guidelines classify patients with heart failure into 1 of 4 stages, A through D.[4] Patients with heart failure risk factors who do not have evidence of structural heart disease are classified as Stage A. Patients with evidence of structural heart disease who have never been symptomatic are classified as Stage B. Patients who are presently or previously symptomatic and responsive to standard therapies are classified as Stage C. Finally, patients are classified as Stage D if they are refractory to standard therapies and require specialized advanced treatment such as mechanical circulatory support, continuous inotropic infusions, or cardiac transplantation. By definition, patients with ADHF have either Stage C or Stage D heart failure.

Early recognition and appropriate treatment are key components in improving the management of these patients.[5–7] Hospitalization is recommended for patients with evidence of severely decompensated heart failure, dyspnea at rest, hemodynamically significant arrhythmias, and acute coronary syndromes and should be considered in patients with worsening congestion, major electrolyte abnormalities, associated comorbid conditions, and repeated implantable cardioverter-defibrillator firings.[8] However, correctly identifying ADHF at the time of hospital presentation can be challenging.[9] The diagnosis of ADHF is based on signs and symptoms, supported by radiographic findings, biomarkers, and echocardiography.[8,10] Unfortunately, the typical signs and symptoms of ADHF—for example, rales, peripheral edema, dyspnea at rest, and fatigue—may be missing at hospital presentation. In an early evaluation, rales, edema, and elevated mean jugular venous pressure were absent in 18 of 43 patients with documented pulmonary capillary wedge pressures (PCWP) $\geq$22 mm Hg.[11] These findings have recently been confirmed using data from 2 large registries, the Acute Decompensated Heart Failure National Registry (ADHERE) and the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry. In these registries, 32%–36% of patients admitted with ADHF did not have rales, 33%–35% did not have peripheral edema, 56%–64% did not have dyspnea at rest, and approximately 67% did not have fatigue (Figure 1).[12,13] Furthermore, even when these signs and symptoms are present, they are nondiagnostic, because they can be produced by a variety of disorders, including hepatic, renal, and pulmonary dysfunction.[8,14]



	Rales	Peripheral edema	Dyspnea at rest	Fatigue
ADHERE N = 67,966	68%	67%	36%	33%
OPTIMIZE-HF N = 48,612	64%	65%	44%	Not Reported

FIGURE 1. Prevalence of rales, peripheral edema, dyspnea at rest, and fatigue in patients admitted for acute decompensated heart failure in the Acute Decompensated Heart Failure National Registry (ADHERE; N = 67,966) and the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure registry (OPTIMIZE-HF; N = 48,612). Derived from Abraham et al[12] and Gheorghiade et al.[13]

Similarly, radiographic and echocardiographic features of ADHF are not always present. Overall, 26% of patients in ADHERE did not have evidence of pulmonary congestion on their initial chest radiograph, and 50%–55% of patients in both registries had preserved systolic function.[13,15–17] Consequently, attention has turned to biomarkers as a means of rapidly and accurately identifying ADHF. Serum B–type natriuretic peptide (BNP) and its N-terminal prohormone (NT-proBNP) have proven to be both diagnostic and prognostic indicators in ADHF.[14,18–25] In the Breathing Not Properly Multinational Study, a BNP level $\geq$100 pg/mL was found to have a 90% sensitivity (95% confidence interval [CI]: 88%–92%) and a 76% specificity (95% CI: 73%–79%) for heart failure in patients presenting to the emergency department with dyspnea.[21] In addition, BNP levels have been shown to correlate with heart failure severity[18] and to be a more accurate reflection of this severity than clinical judgment.[23] In a prospective randomized evaluation, the addition of BNP assessment to a standard diagnostic evaluation resulted in fewer patients being hospitalized (75% vs. 85%; $P = .008$), more rapid initiation of appropriate therapy (63 vs. 90 minutes; $P = .03$), and a shorter median duration of hospitalization (8 vs. 11 days; $P = .001$).[26] As a result, the American

College of Emergency Physicians guidelines now state that measurement of BNP or NT-proBNP can improve diagnostic accuracy in acute heart failure syndrome when compared with standard clinical judgment alone.[27]

It is important to remember, however, that BNP levels cannot be interpreted in isolation; clinical judgment still plays a vital role. Obesity decreases BNP levels due to the expression of natriuretic peptide clearance receptors in adipose tissue.[9,28,29] In contrast, BNP levels increase with age and are higher in women than in men.[29] In addition, pulmonary embolism, an important diagnostic consideration in patients presenting with dyspnea, has been shown to increase serum BNP levels above the diagnostic threshold for ADHF.[9,29] Likewise, renal dysfunction, a common comorbidity in patients with heart failure (cardiorenal syndrome), increases serum BNP levels.[30] As a result, the BNP threshold value for the diagnosis of ADHF rises from 100 pg/mL in patients with normal renal function to 200 pg/mL in patients with an estimated glomerular filtration rate <60 mL/min/1.73 m^2.[30] Finally, it is now well recognized that BNP production is up-regulated by numerous physiologic conditions in addition to heart failure, including cardiac hypertrophy, endothelial dysfunction, and arrhythmia.[31] Consequently, an elevated BNP level may indicate one of these conditions instead of ADHF. For example, recent data demonstrate that BNP levels are increased in patients with acute coronary syndromes and also serve as a significant prognostic factor in these patients.[32,33]

RISK STRATIFICATION

Risk stratification, another important component in improving the management of patients with ADHF, helps determine the appropriate location (eg, outpatient, hospital ward, intensive care unit) for and intensity of initial monitoring and treatment.[13,25,34–52] Univariate analyses have identified several morbidity and/or mortality risk factors, including age,[35–40] blood pressure,[13,34,37,39–41] respiratory rate,[37] left ventricular ejection fraction (LVEF),[36,41,48] renal function,[34,36,37,39,40,42,43] anemia,[25,44,45] hyponatremia,[37,39,46] BNP level,[36,49,50] cardiac troponin level,[48] diuretic dose,[36,49,50] previous heart failure hospitalization,[44,51,52] and comorbid conditions.[35,37,39] Unfortunately, these univariate factors are not very helpful in and of themselves, as they regularly occur in conjunction with each other. True risk assessment requires multivariate analyses of large datasets.

TABLE 1
Multivariate Risk Factors in Patients Admitted for Acute Decompensated Heart Failure

	Study		
Parameter	**Lee et al[37]**	**Fonarow et al[34]**	**Rohde et al[39]**
Data source	34 Hospitals	263 Hospitals	Single center
Admissions evaluated	4031	65,275	779
Outcome parameter	30-Day mortality	In-hospital mortality	In-hospital mortality
Independent risk factors			
Older age	Yes	Yes	Yes (>70 years)
Lower SBP	Yes	Yes (<115 mm Hg)	Yes (≤124 mm Hg)
Renal dysfunction	Yes	Yes	Yes
Elevated BUN	Yes	Yes (>43 mg/dL)	Yes (>37 mg/dL)
Elevated serum creatinine		Yes (>2.75 mg/dL)	Yes (>1.4 mg/dL)
Hyponatremia	Yes		Yes (<136 mEq/L)
Elevated heart rate		Yes	
Elevated respiratory rate	Yes		
Comorbid conditions	Yes		Yes
Cancer	Yes		Yes
Cerebrovascular disease	Yes		
COPD	Yes		
Dementia	Yes		

Abbreviations: BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; SBP, systolic blood pressure.

Multivariate risk factors for short-term mortality in patients admitted for ADHF have been evaluated in 3 separate studies. Lee et al used multiple logistic regression to analyze data from 4031 hospitalization episodes at 34 centers in Canada,[37] Fonarow et al used both classification and regression tree and multivariate regression models to analyze data from 65,275 hospitalization episodes at 263 centers in the United States,[34] and Rohde et al used stepwise logistic regression to analyze data from 779 consecutive hospitalization episodes at a single center in Brazil.[39] Despite these differences in statistical methodology and geographic location, the findings of these 3 analyses are remarkably similar. All 3 evaluations identified advanced age, lower systolic blood pressure, and renal dysfunction (cardiorenal syndrome) as significant and independent risk factors for short-term mortality, and 2 of the 3 identified hyponatremia and comorbid cancer as additional risk factors (Table 1).[34] Of note, lower systolic blood

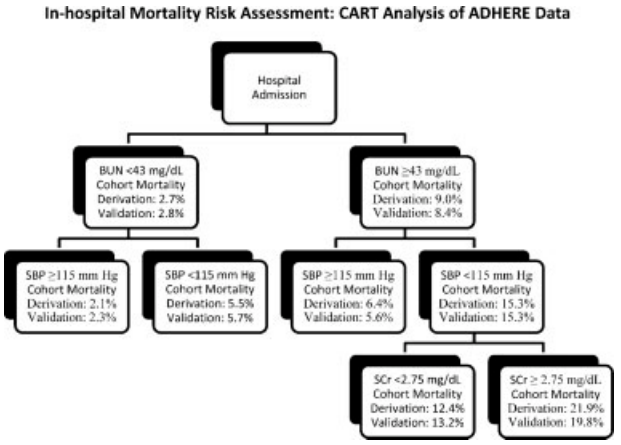


FIGURE 2. Risk of in-hospital mortality based on Classification and Regression Tree Analysis (CART) of data from the Acute Decompensated Heart Failure National Registry (ADHERE). The model was developed using data from the initial 33,046 hospitalizations in the registry (Derivation cohort) and validated using data from the subsequent 32,229 hospitalizations (Validation cohort). Abbreviations: BUN, blood urea nitrogen; SBP, systolic blood pressure; SCr, serum creatinine. Adapted from Fonarow et al.[34]

pressure did not mean hypotension in these evaluations. Mortality risk was significantly increased in patients with systolic blood pressure <115-124 mm Hg. In the largest of these studies, a simple risk tree utilizing admission blood pressure, serum creatinine concentration, and blood urea nitrogen level stratified patients into groups with in-hospital mortality risk ranging from 2.1%–21.9% in the derivation and 2.3%–19.8% in the validation cohorts (Figure 2).[34] Taken together, these studies underscore the substantial role age, blood pressure, renal function, serum sodium concentration, and comorbidities play in increasing mortality risk, and these factors should always be considered in determining the intensity and location of ADHF treatment and degree of monitoring employed therein.

Although BNP and cardiac troponin level were not significant risk factors in the multivariate models, these levels were not routinely assessed in patients admitted for ADHF 5 to 10 years ago. For example, admission BNP was available in only 18% of patients in the Fonarow analysis,[34] and this lack of data may explain the absence of these parameters in these multivariate analyses. In a recent analysis limited to patients with admission BNP and cardiac troponin data, in-hospital mortality was significantly increased when BNP was ≥840 pg/mL (odds ratio [OR]: 1.60; 95% CI: 1.43–1.80; $P < .001$), cardiac troponin was positive (OR: 1.85; 95% CI: 1.57–2.18; $P < .001$) or both (OR: 3.00; 95% CI: 2.47–3.66; $P < .001$) even after adjusting for differences in age, gender, blood urea nitrogen, systolic blood pressure, serum creatinine concentration, serum sodium concentration, heart rate, and dyspnea at rest.[4]

THERAPY

Ideally, treatment should be rooted in evidence-based guidelines. However, relatively few randomized, controlled clinical trials have been completed in patients with ADHF, and consequently there are minimal data available to construct these guidelines. The American College of Cardiology and the American Heart Association have jointly published guidelines since 1995 on the management of heart failure.[4,53] However, these guidelines, which were last updated in 2005, discuss only the management of chronic heart failure, not the management of ADHF.[4] In fact, the most recent version of these guidelines specifically states, "The committee elected to focus this document … on the diagnosis and management of chronic heart failure … It specifically did not consider acute heart failure, which might merit a separate set of guidelines."[4]

The first guideline to specifically address the management of ADHF was published in 2004.[5] These guidelines, a consensus statement based on expert panel review of the available literature, were created to improve treatment at member hospitals of a national group purchasing organization and focused only on the initial 24 hours of care. They had 2 important components. The first was a timeline emphasizing rapid assessment and institution of therapy, followed by serial reevaluations every couple of hours thereafter.[5] The second was a flow chart detailing recommended initial therapies based on the current clinical findings and the patient's chronic outpatient pharmacotherapy, followed by modifications to this initial therapy based on the response observed during the serial reevaluations. Treatment recommendations were as follows: for patients with mild volume overload, an intravenous diuretic; for patients with moderate to severe volume overload, an intravenous diuretic plus an intravenous vasodilator (nitroglycerin or nesiritide); and for patients with low cardiac output, an inotropic

agent with or without a subsequent intravenous vasodilator.

In 2005, the European Society of Cardiology published its guidelines for the treatment of ADHF.[10] These guidelines state that the immediate goal of ADHF therapy is to improve symptoms and stabilize hemodynamics, but these short-term benefits must be accompanied by favorable effects on long-term outcomes.[10] Recommended treatment consists of fluid loading, diuretics, vasodilators (glyceryl trinitrate, isosorbide dinitrate, nitroprusside, or nesiritide), and/or inotropic agents (dopamine, dobutamine, milrinone, enoximone, levosimendan, norepinephrine, or epinephrine), depending on the patient's clinical status and hemodynamics.[10] In general, the guidelines recommend fluid loading in patients with low cardiac output and low PCWP; a vasodilator or inotropic agent, depending on systolic blood pressure, in patients with low cardiac output and normal to high PCWP; and an intravenous diuretic in patients with normal cardiac output and high PCWP pressure. Finally, respiratory support, eg, continuous positive airway pressure (CPAP), noninvasive positive pressure ventilation, or endotracheal intubation and mechanical ventilation, may be necessary in some patients with left-heart failure.

In 2006, the Heart Failure Society of America published comprehensive heart failure practice guidelines.[8] These guidelines expand the goals of ADHF therapy to include improving symptoms, optimizing volume status, identifying precipitating factors, enhancing chronic oral therapy, and minimizing side effects. They provide the most detailed recommendations yet with respect to monitoring patents admitted for ADHF.[8] According to these guidelines, this monitoring should include "more than daily" assessment of vital signs, including orthostatic blood pressure, and "at least daily" assessment of heart failure signs and symptoms, fluid intake and output, weight, electrolytes, and renal function. Treatment recommendations are similar to those in preceding guidelines. Intravenous loop diuretics are recommended as first-line therapy in patients with volume overload.[8] In the absence of systemic hypotension, the addition of an intravenous vasodilator (nitroglycerin, nitroprusside, or nesiritide) should be considered to achieve rapid symptomatic improvement.[8] Intravenous inotropic therapy may be considered to improve symptoms and end-organ function in patients with low-output syndrome (left ventricular dilation, reduced LVEF, and diminished peripheral perfusion), especially if systolic blood pressure is <90 mm Hg or there is symptomatic hypotension despite adequate filling pressures.[54] Outside of this small select group of patients, there is no rationale for the use of inotropic agents.[8] Patients with ADHF who received an inotropic agent in the absence of a clearly defined clinical indication had an increased risk of adverse events without any evidence of clinical benefit in the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) trial.[54] Ultrafiltration may be considered in patients who fail to respond adequately to diuretic therapy,[6,8] and an implantable left ventricular assist device (LVAD) should be considered as a bridge to cardiac transplantation in patients with severe heart failure (Stage D) who have become refractory to all means of medical circulatory support and may be considered in highly selected nontransplantation candidates who cannot be weaned from intravenous inotropic support.[8,52]

Whether to continue or temporarily stop chronic oral heart failure medications during treatment of an acute decompensation is not addressed in any of the evidence-based guidelines and ultimately, this decision must be based on the patient's clinical status. In general, guideline-recommended intravenous diuretic therapy temporarily replaces the patient's chronic oral diuretic regimen. Oral β-blocker therapy should be continued whenever possible, as long as the patient's blood pressure and clinical status can tolerate it. In an analysis of data from the OPTIMIZE-HF registry, patients with ADHF who had withdrawal of β-blocker had significantly greater risk-adjusted mortality compared to those in whom this therapy was continued (hazard ratio: 2.3; 95% CI: 1.2-4.6; $P = .013$).[55,56] Finally, it is recommended that patients receiving an angiotensin-converting enzyme inhibitor be continued on this agent as long as they are not in cardiogenic shock and do not have significantly deteriorating renal function.[8]

ROLE OF THE HOSPITALIST

Despite the presence of treatment guidelines, significant variation in the treatment of patients with ADHF persists.[8,58] Treatment of these patients is frequently contrary to the recommendations in

published guidelines and can adversely impact both the cost of hospitalization and the ultimate clinical outcome. Low adherence to accepted standards of medical care has been shown to be a significant and independent risk factor for early hospital readmission.[58] Furthermore, the main determinant of inotrope use in the ESCAPE trial was not the patient's cardiac output, blood pressure, or PCWP, but instead was the hospital to which the patient was admitted.[59]

Hospitalists are positioned to play a key role in improving both inpatient care of ADHF patients and the transition to long-term patient management.[60,61] However, specific core competencies are required before hospitalists can effectively undertake this role. Table 2 highlights some of these core competencies.[57]

Data indicate that hospitalists are more likely than nonhospitalists to implement evidence-based assessments and treatment.[62] Lindenauer et al conducted a retrospective review of medical records from patients admitted for ADHF at a community-based teaching hospital who were not managed by cardiologists and found that the assessment of left ventricular function was significantly greater when the patient's care was managed by a hospitalist (94%) compared to a nonhospitalist (87%; $P = .04$).[61] Similarly, Roytman et al performed a retrospective review of medical records from another community-based teaching hospital and found that patients admitted for ADHF who were managed by hospitalists were more likely than patients managed by community physicians (55% cardiologists) to receive intravenous diuretics (90% vs. 73%; $P < .001$) and to have angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy initiated or resumed within 24 hours of hospital admission (86% vs. 72%; $P = .003$).[62]

Hospitalist care has also been shown to significantly reduce the duration of hospitalization. In the evaluation by Lindenauer et al, the risk-adjusted length of stay was significantly shorter in patients whose care was managed by a hospitalist ($P = .03$). This benefit was greatest for patients in the major severity category.[61] Similarly, in the review by Roytman et al, hospitalist care was associated with a 13%–40% reduction in adjusted length of stay ($P = .002$), depending on disease severity.[62] These reductions appear to be directly related to the greater experience of hospitalists in managing this and other acute disorders. In a retrospective review of data from an urban teaching hospital, care by a hospitalist, when compared with that by a nonhospitalist, was associated with a 15% reduction in overall length of stay (5.0 vs. 5.9 days; $P < .02$), with the greatest benefit observed in those patients whose disorders required close clinical monitoring (ie, heart failure, stroke, asthma, or pneumonia) or complex discharge planning.[63] Moreover, there was a significant inverse correlation between the mean duration of hospitalization and the number of months of inpatient care provided by the attending physician each year ($\beta = -0.19$ day per month of inpatient care; $P < .002$).[63]

Finally, hospitalists are uniquely situated to influence medical care. Hospitalists have the ability to closely interact with patients over the course of several days. This exposure enhances opportunities to provide and reinforce patient education and information on lifestyle modifications, which have been shown to reduce the frequency of rehospitalization.[60] In one evaluation, initiation of a care-management program that included

TABLE 2
Selected Core Competencies for Hospitalists in Management of Heart Failure

Domain	Competencies
Knowledge	Underlying causes of heart failure (eg, ischemia, cardiomyopathy, arrhythmia, drugs, alcohol)
	Precipitating factors leading to exacerbation (eg, fluid overload)
	Indicated tests to evaluate heart failure (eg, chest x-ray, echocardiography, B-type natriuretic peptide levels)
	Risk factors for the development of heart failure (eg, hypertension, hyperlipidemia, coronary artery disease, diabetes, obesity)
	Risk stratification in patients admitted with heart failure
	Evidence-based therapeutic options for management of both acute and chronic heart failure
	Indications, contraindications, and mechanisms of action of drugs used to treat heart failure
Skills	Identify signs of low perfusion (eg, capillary refill, end-organ dysfunction)
Attitudes	Recognize indications for cardiac consultation (eg, ischemia, atypical presentation, unresponsive to usual therapy)
	Recognize indications for transplantation evaluation (eg, uncontrollable severe heart failure)
System organization and improvement	Advocate establishment and support of outpatient heart failure management teams

Adapted from the Journal of Hospital Medicine.[57]

increased patient education reduced rehospitalizations for heart failure by 85% ($P < .001$).[64] In another, an intensive, targeted education program significantly decreased the 1-year risk-adjusted probability of readmission or death (hazard ratio: 0.56; 95% CI: 0.32-0.96; $P = .03$).[65] Finally, it is important to remember that hospitalists also play a key role in the education of medical students and residents.[60] This opportunity permits hospitalists to promote the adoption of standardized treatment algorithms that hopefully will be retained and propagated by these students long after their initial exposure to the hospitalist, thereby magnifying the effects of this education.

Address for correspondence and reprint requests: Alpesh Amin, MD, MBA, FACP, Professor and Chairman, Department of Medicine, Executive Director, Hospitalist Program, University of California, Irvine, 101 The City Drive South, Building 26, Room 1005 ZC-4076H Orange, CA 92868; Telephone: (714) 456-3785; Fax: (714) 456-7182; E-mail: anamin@uci.edu

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