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Clinical Assessment Identifies Hemodynamic Profiles That Predict Outcomes in Patients Admitted With Heart Failure

Anju Nohria, MD, Sui W. Tsang, BS, James C. Fang, MD, Eldrin F. Lewis, MD, John A. Jarcho, MD, Gilbert H. Mudge, MD, Lynne W. Stevenson, MD

Boston, Massachusetts

OBJECTIVES This study was designed to determine the relevance of a proposed classification for advanced heart failure (HF). Profiles based on clinical assessment of congestion and perfusion at the time of hospitalization were compared with subsequent outcomes.

BACKGROUND Optimal design of therapy and trials for advanced HF remains limited by the lack of simple clinical profiles to characterize patients.

METHODS Prospective analysis was performed for 452 patients admitted to the cardiomyopathy service at the Brigham and Women's Hospital with a diagnosis of HF. Patients were classified by clinical assessment into four profiles: profile A, patients with no evidence of congestion or hypoperfusion (dry-warm, n = 123); profile B, congestion with adequate perfusion (wet-warm, n = 222); profile C, congestion and hypoperfusion (wet-cold, n = 91); and profile L, hypoperfusion without congestion (dry-cold, n = 16). Other standard predictors of outcome were included and patients were followed for the end points of death (n = 117) and death or urgent transplantation (n = 137) at one year.

RESULTS Survival analysis showed that clinical profiles predict outcomes in HF. Profiles B and C increase the risk of death plus urgent transplantation by univariate (hazard ratio [HR] 1.83, p = 0.02) and multivariate analyses (HR 2.48, p = 0.003). Moreover, clinical profiles add prognostic information even when limited to patients with New York Heart Association (NYHA) class III/IV symptoms (profile B: HR 2.23, p = 0.026; profile C: HR 2.73, p = 0.009).

CONCLUSIONS Simple clinical assessment can be used to define profiles in patients admitted with HF. These profiles predict outcomes and may be used to guide therapy and identify populations for future investigation. (J Am Coll Cardiol 2003;41:1797–804) © 2003 by the American College of Cardiology Foundation

As new treatments for heart failure (HF) emerge, there is an urgent need to identify the appropriate patient for each therapy. The spectrum of patients hospitalized with advanced to severe HF presents particular challenges. In clinical trials, these patients range from those for whom routine use of intravenous inotropic therapy has no impact on outcome (1) to those who need a left ventricular assist device (LVAD) to improve their annual survival from 25% to 52%, despite palliative intravenous inotrope use in 72% (2).

Indicators of disease severity have been used to stratify patients. Some precise parameters such as peak oxygen consumption are complex to obtain and most useful in moderate rather than acutely decompensated HF. Other indicators such as the New York Heart Association (NYHA) symptom classification are subjective and difficult to separate from concomitant disease conditions. Many laboratory values such as neurohormonal markers and renal indices, although useful in large populations, do not provide clear thresholds for the intensification of therapy in an individual patient. Therefore, most physicians rely upon the clinical history and physical examination to assess and guide therapy in this patient population.

In 1976, Forrester et al. (3) demonstrated that among patients who had an acute myocardial infarction (AMI), the physical examination identified four hemodynamic profiles defined by Swan-Ganz catheterization. These profiles were based on the presence or absence of congestion (pulmonary capillary wedge pressure [PCWP] > or ≤18 mm Hg) and adequacy of perfusion (cardiac index [CI] >2.2 l/min/m^2). Profile I represented no congestion or hypoperfusion; profile II, congestion without hypoperfusion; profile III, hypoperfusion without congestion; and profile IV, both congestion and hypoperfusion. Furthermore, both the clinical and invasive hemodynamic profiles predicted short-term survival, with increased mortality when congestion was present and even worse outcomes when both congestion and hypo-

From the Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts. Dr. Nohria received salary support from the Clinical Investigator Training Program, Boston, Massachusetts, co-sponsored by Beth Israel Deaconess Medical Center, Harvard-M.I.T. Division of Health Sciences and Technology, and Pfizer, Inc. The Brigham and Women's Hospital Heart Failure/Transplant Program received financial support from the William T. Young Corporation of Lexington, Kentucky, and the Fannie Rippel Foundation, Baskin Ridge, New Jersey.

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Abbreviations and Acronyms

AMI	= acute myocardial infarction
CI	= cardiac index
ESCAPE	= Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization
HF	= heart failure
HR	= hazard ratio
LVAD	= left ventricular assist device
NYHA	= New York Heart Association
PCWP	= pulmonary capillary wedge pressure
REMATCH	= Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure
SOLVD	= Studies Of Left Ventricular Dysfunction
UNOS	= United Network of Organ Sharing

perfusion were evident (3). Physical findings (such as rales and peripheral edema) used to determine profiles after an AMI are often inadequate for the detection of elevated filling pressures in chronic HF (4). However, other components of the clinical evaluation (such as orthopnea and proportional pulse pressure) correlate well with hemodynamics in chronic HF (4). It remains to be shown whether definition of hemodynamic profiles, based on the history and physical examination, provides meaningful distinction among patients with chronic HF.

Our study tested the hypothesis that the four clinical profiles, determined by evidence of congestion and adequacy of perfusion on clinical examination, define prognostic categories in patients admitted with a history of HF.

METHODS

Patient population. This analysis included 452 consecutive hospitalized patients referred to the cardiomyopathy service at Brigham and Women's Hospital between November 1996 and July 1999 with a new or prior diagnosis of HF. Among these patients, the primary admitting diagnosis was decompensated HF in 49%, arrhythmia in 12%, angina in 12%, elective transplant evaluation for chronic HF in 17%, and other issues, such as infection, in 6%. Baseline characteristics of the patient population are shown in Table 1. Patient information was obtained from the medical record and the Social Security Death Index. Brigham and Women's Hospital's Human Research Committee approved this study.

Assessment of clinical profiles. Physicians (faculty or fellows) on the cardiomyopathy service evaluated and prospectively classified patients within 24 h of admission into four hemodynamic profiles based on the clinical examination. Physicians also prospectively assessed NYHA functional class based on the patients' reported functional limitation. The clinical profiles were defined by: 1) the absence or presence of signs of congestion, and 2) evidence suggesting adequate or inadequate perfusion (Fig. 1). Indications of congestion included a recent history of orthopnea and/or physical exam evidence of jugular venous distention, rales, hepatojugular reflux, ascites, peripheral edema, leftward radiation of the pulmonic heart sound, or a square wave blood pressure response to the Valsalva maneuver. Compromised perfusion was assessed by the presence of a narrow proportional pulse pressure ([systolic − diastolic blood pressure]/systolic blood pressure <25%), pulsus alternans, symptomatic hypotension (without orthostasis), cool extremities, and/or impaired mentation. Physicians synthesized the presence or absence of any or all of these signs to make a subjective assessment of the patients' volume and perfusion status. Physicians were not required to justify their assignment of clinical profile, nor was their classification verified or altered by the authors of this study.

Survival estimates. Patients were followed for at least one year after the index admission with a mean follow-up of 18 ± 13 months. Survival for each profile was estimated for the end points of: 1) death without transplantation, and 2) either death without transplantation or urgent transplanta-

Table 1. Baseline Characteristics of the Patient Population

Characteristics	Values
Total patients, n	452
Men/women, n/n (%,%)	313/139 (69/31)
Mean age ± SD, yrs	55.4 ± 14.2
Mean ejection fraction ± SD, %	25.8 ± 11.8
Etiology of heart failure	
Ischemic cardiomyopathy, n (%)	222 (49)
Dilated cardiomyopathy, n (%)	118 (26)
Other, n (%)	112 (25)
Medications on admission	
ACEI or ARBs, n (%)	331 (73)
Digoxin, n (%)	301 (67)
Diuretics, n (%)	362 (80)
Beta-blockers, n (%)	116 (26)

ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers.

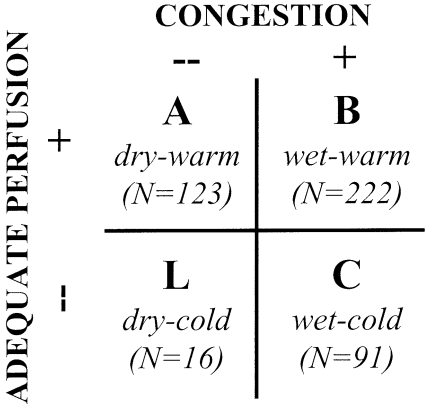


Figure 1. Schematic for assessment of clinical profiles. Congestion was assessed by the presence of orthopnea, jugular venous distention, rales, hepatojugular reflux, ascites, peripheral edema, leftward radiation of the pulmonic heart sound, or a square-wave blood pressure response to the Valsalva maneuver. Compromised perfusion was assessed by the presence of a narrow proportional pulse pressure, pulsus alternans, symptomatic hypotension (without orthostasis), cool extremities, and/or impaired mentation.

Table 2. Baseline Characteristics of Patients According to the Clinical Profile

Characteristics	Clinical Profiles				p Values
	A (n = 123)	B (n = 222)	C (n = 91)	L (n = 16)	
Age, yrs	55 ± 14	56 ± 15	55 ± 13	50 ± 13	0.30
Male gender, %	73	67	71	56	0.41
Ischemic cardiomyopathy, %	53	46	53	44	0.53
Time since first diagnosis, months	14 ± 22	22 ± 32	11 ± 17	27 ± 46	0.14
Medications					
ACEI or ARB, %	78	74	65	75	0.19
Digoxin, %	68	68	64	56	0.72
Diuretics, %	80	82	76	81	0.66
Beta-blockers, %	35	23	19	22	0.04
Ejection fraction, %	28.2 ± 11.0	26.3 ± 12.9	21.5 ± 9.5	23.6 ± 7.3	0.0004
NYHA functional class	2.3 ± 0.9	3.1 ± 0.7	3.5 ± 0.8	2.9 ± 0.9	< 0.0001
Resting heart rate, beats/min	81 ± 16	88 ± 18	91 ± 21	81 ± 20	0.0004
Systolic blood pressure, mm Hg	116 ± 23	114 ± 21	103 ± 17	101 ± 15	< 0.0001
Serum sodium, mEq/l	138 ± 4	137 ± 5	136 ± 5	137 ± 5	0.01
Serum creatinine, mg/dl	1.3 ± 1.0	1.4 ± 0.8	1.5 ± 1.0	1.3 ± 1.0	0.40
PCWP (n = 53), mm Hg	15.6 ± 7.9	26.7 ± 6.0	32.3 ± 6.9	30.3 ± 4.0	< 0.0001
CI (n = 50), mm Hg	2.3 ± 0.3	2.1 ± 0.6	1.9 ± 0.7	1.6 ± 0.5	0.07

*Plus-minus values are means ± SD.
ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; CI = cardiac index; NYHA = New York Heart Association; PCWP = pulmonary capillary wedge pressure.

tion at one year. Urgent transplantation was defined as United Network of Organ Sharing (UNOS) status 1 (receiving intravenous inotropic or mechanical support up until the time of transplantation). The follow-up rate was 99.5%.

Statistical analysis. All data are expressed as mean ± SD. Comparisons of parameters between profiles were made by Fisher's exact test or one-way ANOVA, followed by a Bonferroni correction for multiple comparisons. A value of $p < 0.08$ was considered significant for individual comparisons. The overall p values reflecting trends between groups are reported rather than p values for individual comparisons. Survival curves were derived by the Kaplan-Meier method and compared using the log-rank test, followed by a Bonferroni correction for multiple comparisons. Profile L was excluded because of the small number of events in this category. Patients who underwent UNOS 2 transplant were censored at transplantation, as were patients who were alive without a transplant at the end of the follow-up period. A value of $p < 0.02$ was considered significant for individual comparisons. The prognostic value of each variable was tested by univariate Cox proportional hazards regression analysis. The prognostic value of the clinical profiles relative to other predictors identified by the univariate analysis was compared using a multivariate model. A value of $p < 0.05$ was considered statistically significant.

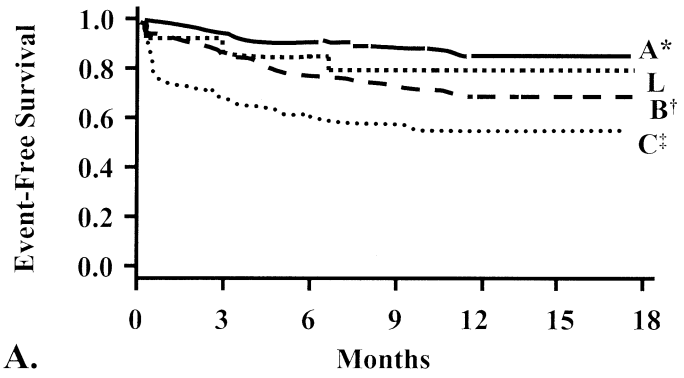
RESULTS

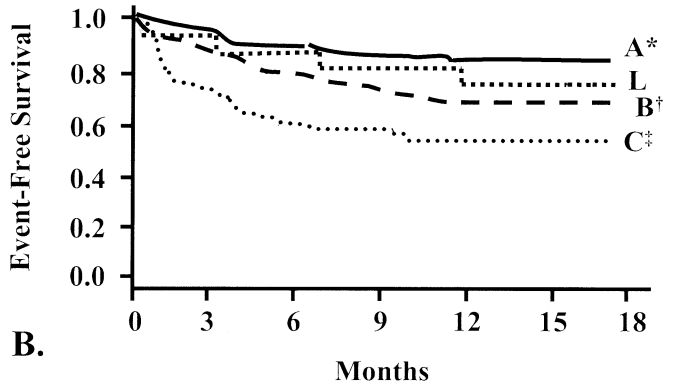
Comparison of patient characteristics by clinical profile. Of the 452 patients, 123 (27%) were classified as profile A (dry-warm), 222 (49%) as profile B (wet-warm), 91 (20%) as profile C (wet-cold), and 16 (4%) as profile L (dry-cold). The limited number of patients with profile L did not allow meaningful comparison of this category. Nonetheless, patients in all four profiles were statistically similar with regard to age, gender, etiology and duration of HF, and medication use other than beta-blockers at the time of admission (Table 2). Other known predictors such as left ventricular ejection fraction (5), NYHA functional class (6), resting heart rate (7), systolic blood pressure (8), serum sodium (9), and serum creatinine (10,11) suggested that patients with profile C (wet-cold) had more advanced HF than those with profile B (wet-warm), who in turn had more severe disease than patients with profile A (dry-warm) (Table 2). Only 40% of patients had peak oxygen consumption measured within six months of hospitalization. The mean peak oxygen consumption for each clinical profile was within 10 to 14 ml/kg/min, with no significant differences between the distinct clinical profiles ($p = 0.244$).

Although right heart catheterization was performed in only 50 of the 452 patients within 24 h of admission, it suggested that clinical profiles reflect invasive hemodynamics (Table 2). Patients with profiles B and C had higher PCWP than patients with profile A ($p < 0.0001$), whereas profile C tended to have lower CI than profiles A and B ($p = 0.07$).

Prognosis by clinical profile. Of the 452 patients, 117 (26%) died without transplantation at one year. An additional 42 (9%) were transplanted within one year, 20 of who were listed as UNOS 1 at the time of transplantation. Kaplan-Meier survival curves for the end-points of death and death plus urgent transplantation according to the clinical profiles are shown in Figure 2. Patients with profile C had a lower survival than profile B ($p < 0.01$). Both profiles B and C conferred a significantly higher mortality than profile A ($p < 0.01$). Limited patient numbers with profile L precluded meaningful statistical analysis of this category.

JACC Vol. 41, No. 10, 2003
May 21, 2003:1797–804





NO. AT RISK							
Profile A	123	117	111	106	101	91	75
Profile B	222	193	167	153	140	122	106
Profile C	91	49	49	45	43	39	30
Profile L	16	15	15	14	13	13	9

Figure 2. Kaplan-Meier survival curves according to the clinical profiles. The end points were one-year mortality **(Panel A)** and one-year mortality plus urgent transplantation **(Panel B)**. In both **panels**, profile C conferred the worst outcomes, followed by profile B, which was worse than profile A. Profile L had too few patients for meaningful statistical analysis. **Panel A:** *$p = 0.002$ for profile A versus profile B, †$p = 0.008$ for profile B versus profile C, ‡$p < 0.001$ for profile A versus profile C. **Panel B:** *$p = 0.002$ for profile A versus profile B, †$p = 0.005$ for profile B versus profile C, ‡$p < 0.001$ for profile A versus profile C.

Univariate and multivariate predictors of mortality. Univariate analysis revealed that patients with profiles B (hazard ratio [HR] 2.10, $p = 0.003$) and C (HR 3.66, $p < 0.001$) were at significantly higher risk for the combined outcome of death or urgent transplantation than patients with profile A (Table 3). Additionally, other known predictors including NYHA class, age (6), ischemic etiology of HF (8,12), serum sodium (9), serum creatinine (10,11), and systolic blood pressure (8) were all associated with an increased risk of death or urgent transplantation at one year in the univariate model (Table 3).

Among the characteristics identified by univariate analysis, profiles B (HR 1.83, $p = 0.02$) and C (HR 2.48, $p = 0.002$) remained independent predictors of mortality or urgent transplantation in the multivariate analysis (Table 4). Age, ischemic cardiomyopathy, and serum creatinine also remained unfavorable in the multivariate analysis (Table 4).

Prognosis by clinical profile and NYHA class. In order to assess whether clinical profiles provided any additional prognostic information beyond functional class, the patient population was further stratified into those with NYHA class I/II (n = 124) and class III/IV (n = 326) symptoms. The majority of patients with NYHA class I/II symptoms had profile A (71/124), followed by profile B (39/124) on clinical assessment. There were only 23 deaths or urgent transplants among NYHA class I/II patients, making the numbers too small for statistical analysis. In contrast, profiles B (182/326) and C (81/326) constituted most of the patients with NYHA class III/IV symptoms. However, a substantial number of patients describing severe symptoms (NYHA class III/IV) were found to have profile A (51/326) on clinical evaluation. Among the patients with NYHA class III/IV symptoms, survival analysis for the combined end point of death or urgent transplantation (n = 113) revealed that profile C tended to confer a worse prognosis than profile B ($p = 0.04$, significance level 0.02 for multiple comparisons), which in turn had a worse outcome than profile A ($p = 0.015$) (Fig. 3). Multivariate analysis restricted to patients with NYHA class III/IV symptoms revealed that both profiles B (HR 2.23, $p = 0.026$) and C (HR 2.73, $p = 0.009$) delineate patients at increased risk for

Table 3. Univariate Predictors of One-Year Mortality Plus Urgent Transplantation

Variables	Hazard Ratio	(95% CI)	p Value
Profile A	Reference	—	—
Profile B	2.10	(1.29–3.43)	0.003
Profile C	3.66	(2.16–6.21)	< 0.001
Profile L	1.98	(0.75–5.24)	0.17
Age	1.03	(1.02–1.04)	< 0.001
Female gender	0.84	(0.58–1.22)	0.36
Ischemic cardiomyopathy	1.90	(1.35–2.68)	< 0.001
Treatment with ACEI	0.73	(0.51–1.05)	0.09
Treatment with beta-blockers	0.92	(0.62–1.36)	0.68
Ejection fraction	0.99	(0.99–1.01)	0.40
NYHA functional class	1.51	(1.23–1.85)	< 0.001
Resting heart rate	1.00	(0.99–1.01)	0.65
Systolic blood pressure	0.99	(0.98–1.00)	0.01
Serum sodium	0.95	(0.92–0.98)	0.001
Serum creatinine	1.27	(1.16–1.40)	< 0.001

ACEI = angiotensin-converting enzyme inhibitor; CI = confidence interval; NYHA = New York Heart Association.

adverse outcomes, whereas profile A identifies those who may do well despite severe symptoms (Table 4).

DISCUSSION

In this article we used clinical assessment, based on the admission physical examination, to define four simple profiles in hospitalized patients with a history of HF. These profiles, which are easily assessed at the bedside, predict outcomes and provide prognostic information in addition to that obtained from other established indices. These clinical profiles may be used to guide therapy and may provide a means for the identification of suitable patient populations for trials of future therapies.

Basis for the prognostic value of clinical profiles. In this cohort of hospitalized patients with HF, clinical profiles distinguish between populations that reflect established prognostic indicators including ejection fraction (5), NYHA class (6), resting heart rate (7), systolic blood pressure (8), and serum sodium (9). Additionally, both univariate and multivariate analyses demonstrate that clinical profiles are independent predictors of mortality and urgent transplantation in patients admitted with a history of HF. In fact, these data suggest that profiles B and C confer a higher relative risk of a bad outcome than other proven prognostic variables, including NYHA functional class (6). However, the basis for the prognostic value of clinical profiles remains unclear.

It is possible that clinical profiles are surrogates for the duration of HF. However, in this cohort there was no correlation between the original diagnosis of HF and time to hospitalization for decompensation, suggesting that profiles A, B, and C do not represent a sequential progression in disease severity.

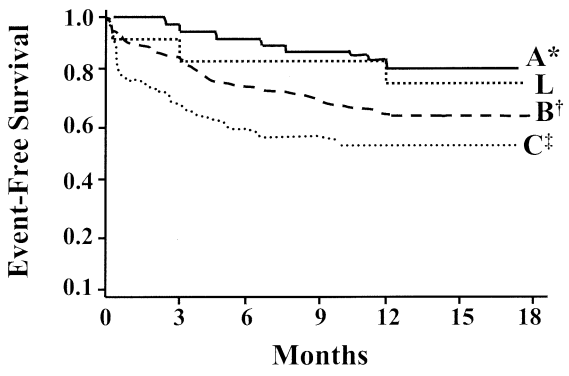
Several studies have shown that hemodynamics predict outcomes in patients with chronic HF (13–16). The small subset of patients who underwent right heart catheterization in this study suggests that clinical profiles may derive prognostic value because they reflect invasive hemodynamic measurements. Several clinical features reliably predict hemodynamic derangements in chronic HF. Orthopnea accurately predicts increased PCWP in 91% of patients with chronic HF (4). Positive hepatojugular reflux also correlates well with elevated PCWP in chronic HF (17–19). An abnormal arterial blood pressure response to the Valsalva maneuver predicts elevated PCWP with a sensitivity of 92% to 100% and a specificity of 83% to 91% (20,21). Additionally, a proportional pulse pressure ≤25% strongly parallels hemodynamic evidence of hypoperfusion (CI ≤2.2 l/min/m^2) (4,22). Because the determination of clinical profiles involves integration of multiple physical findings, clinical profiles may provide a more reliable estimate of invasive hemodynamics than any one sign alone.

A previous study (22) comparing retrospectively assigned clinical profiles to invasive hemodynamics showed that patients with a "wet" profile tended to have higher PCWP than those with a "dry" profile. Similarly, patients with a "cold" profile tended to have lower CI than patients with a "warm" profile. Although outcomes did not differ significantly between the various clinical profiles (22), the trend for survival was similar to that seen in the present analysis.

Table 4. Multivariate Analysis of the Variables Associated With One-Year Mortality Plus Urgent Transplantation

	All Patients		NYHA III/IV	
Variables	Hazard Ratio	p Value	Hazard Ratio	p Value
Profile A	Reference	—	Reference	—
Profile B	1.83	0.02	2.23	0.03
Profile C	2.48	0.003	2.73	0.009
Profile L	1.94	0.19	1.94	0.28
Age	1.02	0.001	1.02	0.004
Ischemic cardiomyopathy	1.52	0.03	1.34	0.15
NYHA functional class	1.25	0.06	1.35	0.13
Systolic blood pressure	0.99	0.09	0.99	0.09
Serum sodium	0.98	0.22	0.99	0.49
Serum creatinine	1.38	< 0.001	1.46	< 0.001

NYHA = New York Heart Association.



NO. AT RISK							
Profile A	51	51	48	45	42	34	26
Profile B	182	153	130	119	108	95	85
Profile C	81	54	44	40	38	35	27
Profile L	12	11	10	10	9	9	6

Figure 3. Kaplan-Meier survival curves according to the clinical profiles in patients with New York Heart Association functional class III/IV heart failure. The end point shown is one-year mortality + urgent transplantation. Patients with profiles B and C had worse outcomes than profile A. Profile L had too few patients for meaningful statistical analysis. The survival for profiles B and C did not differ significantly after Bonferroni correction. *$p = 0.015$ for profile A versus profile B, †$p = 0.04$ for profile B versus profile C, ‡$p < 0.001$ for profile A versus profile C.

Retrospective assignment of profiles and frequent intravenous inotrope use might have made the identification of significant mortality differences between the clinical profiles difficult in the prior study.

Clinical evidence of elevated filling pressures has previously been shown to predict outcomes in HF. A recent report demonstrated that the presence of an elevated jugular venous pressure and S_3 was associated with an increased risk of hospitalization and death among patients enrolled in the Studies Of Left Ventricular Dysfunction (SOLVD) treatment trial (23). Another study evaluating patients four to six weeks after treatment for NYHA class IV symptoms also showed that persistent evidence of congestion predicted worse outcomes in patients with chronic HF (24). Furthermore, objective exercise limitation, which predicts outcomes in patients with chronic HF (25), has also been shown to correlate with physical findings of congestion (26). These results reinforce the value of evaluating disease severity by means of a simple bedside clinical evaluation.

The use of clinical profiles to guide therapy. Although not routinely measured, these data suggest that clinical profiles may provide a qualitative estimate of hemodynamics at the bedside. In the absence of more rigorous evidence, these profiles may help guide therapy. Profile A (dry-warm) described a group of well-compensated patients with a good overall prognosis. Yet, one-third (38/123) of patients with profile A presented with symptoms of decompensated HF, and presentation with profile A may prompt a search for other causes of dyspnea. Because symptom relief and lowering of filling pressures is the immediate goal of therapy in patients with profile B (wet-warm), they may be diuresed empirically, with or without enhanced vasodilation. Conversely, patients with profile C (wet-cold) might require hospitalization for more intensive therapy to achieve adequate diuresis, perhaps even guided by serial invasive hemodynamic measurements. A recent trial evaluating the effects of short-term milrinone on length of hospitalization and 60-day mortality showed that routine use of inotropic therapy in patients with NYHA class III/IV symptoms results in increased short-term morbidity (1). It is possible that profile C may identify a subset of patients within those with NYHA class III/IV symptoms in whom the risk-benefit ratio of short-term inotropic therapy differs.

Clinical profiling may also help guide titration of beta-blocker therapy. Patients with profile A may tolerate initiation and up-titration of beta-blockers with the success observed in major trials, whereas profile B might represent a population where chronic beta-blocker therapy could be maintained but initiation or up-titration deferred until restoration of profile A. Conversely, determination of profile C might lead to a decrease or withdrawal of recently initiated beta-blockers until better compensation is achieved. The greater use of beta-blockers on admission in patients with profile A relative to those with profiles B and C is consistent with this management strategy.

The prognostic information provided by clinical profiles may also help guide listing for transplantation in patients where oxygen consumption measures do not provide an obvious mortality benefit with transplantation (25). In this cohort, the mean peak oxygen consumption ranged from 10 to 14 ml/kg/min, regardless of clinical profile. Thus, in hospitalized patients who are too sick to do an exercise stress test or whose last reported oxygen consumption does not reflect their present clinical status, clinical profiles may be useful.

Although we propose ways in which clinical profiles might be used to guide the treatment of chronic HF, there are no data to support their utility for this indication. This question will be partially addressed by the ongoing multicenter Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) evaluating the correlation of clinical profiles to hemodynamic measurements and the success of clinical assessment-based versus catheter-guided therapy (27).

Similar to prior reports (4,22), profile L (dry-cold) was uncommon in this cohort. This grouping probably represents the few patients with HF who have significantly reduced cardiac reserve with a decreased tendency towards congestion. Alternatively, it might describe patients with severely dilated ventricles and anatomic mitral regurgitation who develop symptoms with minimal exertion. Patients with profile L, in particular, may benefit from interventions such as biventricular pacing, mitral valve repair, and surgical ventricular remodeling aimed at improving myocardial efficiency.

Table 5. Comparison of Mortality for Clinical Profiles to Mortality in Trials of Hospitalized Patients With Advanced Heart Failure

	Profile A	VMAC	OPTIME	Profile B	CONSENSUS*	FIRST	Profile C	REMATCH
SBP, mm Hg	116	121	120	114	119	105	103	103
LVEF, %	28	26	24	26	—	18	22	17
Sodium, mEq/l	138	—	138	137	138	137	136	135
Cr, mEq/l	1.3	1.5	1.5	1.4	1.5	—	1.5	1.8
%6 month mortality	11	23	10 (2 months)	22	29	37	40	46

*Mortality reported for control groups of major trials except CONSENSUS where the mortality for the treatment arm is reported.

Cr = serum creatinine; CONSENSUS = Cooperative North Scandinavian Enalapril Survival Study (32); FIRST = Flolan International Randomized Survival Trial (31); LVEF = left ventricular ejection fraction; OPTIME = Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (1); REMATCH = Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (2); SBP = systolic blood pressure; VMAC = Vasodilation in the Management of Acute CHF (33).

Use of clinical profiles to identify patient populations for research studies. Although the mortality for mild to moderate HF, as defined by NYHA classification, is fairly consistent across trials, advanced HF represents a heterogeneous group of patients with annual mortality estimates ranging from 17% in the beta-blocker trials (28,29) to 75% in the recent LVAD trial (2). This heterogeneity holds true even when restricted to trials of patients hospitalized with advanced HF (Table 5). In this study, whereas the majority of patients with NYHA class III/IV symptoms had profiles B and C, a substantial number had profile A and a relatively good prognosis. A comparison of mortality estimates in large clinical trials of advanced HF to survival for the different clinical profiles suggests that profile A has a similar mortality as the beta-blocker trials (28,29) and profile B to that reported in trials of oral and intravenous inotropic therapy (28,30). The mortality for profile C is similar to that described in the trial of epoprostenol in patients with documented CI $\leq$2.2 l/min/m^2 and PCWP $\geq$15 mm Hg and approaches the early mortality seen in the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial (2) (Table 5). Clinical profiles therefore further stratify patients with advanced HF and could be used to refine inclusion criteria for the selection of patients for investigational therapies.

Study limitations. This analysis has several potential limitations. The results of this single-center study might not be replicated in other settings with less attention to the physical examination. However, in this study, physicians at various levels assessed the clinical profiles, suggesting that these findings might be generalized to others dedicated to the care of this population.

Although physicians were instructed to base their assessment of clinical profiles on the physical examination, other factors such as patient distress or abnormal laboratory values might have influenced their decisions. This potential source of bias has been diminished by controlling for other clinical and laboratory predictors of mortality in the multivariable analysis. Furthermore, the finding that clinical profiles were useful even among patients with NYHA class III/IV symptoms suggests that knowledge of functional capacity did not negate the value of bedside clinical evaluation.

The decision to list patients for transplantation may have been influenced by the clinical profile assessment. Analyses using the end point of death in addition to the combined end points of death and urgent transplantation were therefore performed. The ability of clinical profiles to predict both death and death plus urgent transplantation makes it unlikely that the end points were biased by initial profile observations.

The clinical profiles were not routinely compared to invasive hemodynamic measurements. Many patients did not undergo right heart catheterization or had it performed after initial diuresis to relieve obvious volume overload. Whether clinical profiles only reflect hemodynamics or also integrate other features of circulatory compromise, classification by clinical profiles provides an important prognostic tool that can be used quickly, conveniently, and more repeatedly than right heart catheterization.

CONCLUSIONS

This study of clinical profiles reaffirms the value of clinical assessment in the daily practice of cardiology, which increasingly includes chronic HF. Clinical profiles are easy to define, predict prognosis, and appear to do so better than traditional markers of disease severity. These profiles may be useful to guide therapy and to select appropriate patients for clinical trials, particularly those designed for patients with a poor prognosis on current medical therapy.

Reprint requests and correspondence: Dr. Lynne W. Stevenson, Cardiovascular Division, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115. E-mail: lstevenson@partners.org.

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