

December 2007

# Prognosis of hospitalized new-onset systolic heart failure in Indo-Asians--a lethal problem

FAHIM H. JAFARY
*Aga Khan University*

MAHESH KUMAR
*Aga Khan University*

IRFAN E. CHANDNA
*Aga Khan University*

# Prognosis of Hospitalized New-Onset Systolic Heart Failure in Indo-Asians—A Lethal Problem

FAHIM H. JAFARY, MD, FACC, MAHESH KUMAR, MD, AND IRFAN E. CHANDNA, MD

*Karachi, Pakistan*

**ABSTRACT**

**Background:** Systolic heart failure (SHF), particularly when requiring hospital admission carries a poor prognosis. There is a paucity of data in Indo-Asians on outcomes of SHF, among whom the burden of cardiovascular disease is consistently rising. The purpose of this study was to determine the frequency and predictors of mortality and morbidity amongst patients admitted with new-onset SHF at a tertiary care hospital in Pakistan.

**Methods and Results:** Hospital charts of 196 patients with a diagnosis of new or recent onset (<3 months) SHF (ejection fraction [EF] <40%) were reviewed. Patients who died during the admission, those with life-limiting concomitant disease, and those without follow-up were excluded. Survival was calculated according to the Kaplan-Meier method. Hazards ratios (HR) and 95% confidence intervals (CI) were calculated using Cox's regression model. Mean age (SD) was 61 (12.8) years. Majority (77%) had a prior ischemic heart disease. Mean EF (SD) was 25% (8.7). Median follow-up period was 379 days. Fifty-four (27.5%) patients died (at least 12 [22.2%] sudden deaths) and 102 (52%) experienced combined event of death or repeat hospitalization for SHF. Factors independently associated with death included (HR [95% CI]), serum sodium (0.94 [0.90−0.97]), admission pulse (1.02 [1.01−1.04]), systolic blood pressure (0.98 [0.97−0.99]), and severe mitral regurgitation (1.90 [1.03−3.48]).

**Conclusions:** Admission for new or recent onset SHF predicts a grave 1-year prognosis in Indo-Asians. Measures to prevent ischemic heart disease and its sequelae are essential because developing nations simply cannot afford to treat and manage heart failure. (*J Cardiac Fail 2007;13:855−860*)

**Key Words:** Heart failure, systolic dysfunction, congestive heart failure, left ventricular dysfunction, developing country.

Congestive heart failure has become an increasingly frequent cause of hospital admission over the last 20 years.[1] Heart failure from systolic dysfunction carries a highly adverse prognosis despite significant advancements in therapy. The 1-year mortality of systolic heart failure in the era of modern heart failure therapy (1990s and beyond) is reported to be 28% in men and 24% in women.[2] These estimates include all-comers with systolic heart failure and do not make a distinction between those with chronic heart failure and those who experience a heart failure−related hospitalization. Hospitalized heart failure is widely regarded as prognostically more adverse with a high mortality and readmission rate.[3] There is a paucity of data on outcomes of heart failure in general and hospitalized heart failure in particular in Indo-Asians. We sought to determine the 1-year morbidity and mortality among patients admitted with new-onset heart failure from systolic dysfunction at a tertiary care hospital in Pakistan. We also endeavored to determine the predictors of mortality and morbidity in this patient group.

## Methods

### Patient Population

This was a retrospective cohort study conducted at the Aga Khan University Hospital in Karachi, Pakistan. The Aga Khan University Hospital is a tertiary care hospital located in the metropolitan city of Karachi and receives a mixture of affluent and low- and middle-income patients and serves the entire city as a referral

*From the Department of Medicine, Section of Cardiology, Aga Khan University Hospital, Karachi, Pakistan.*

Manuscript received March 7, 2007; revised manuscript received July 9, 2007; revised manuscript accepted July 17, 2007.

Reprint requests: Fahim H. Jafary, MD, FACC, Associate Professor and Consultant Cardiologist, Department of Medicine, Section of Cardiology, Aga Khan University Hospital, PO Box 3500, Stadium Road, Karachi 74800, Pakistan.

Conflict of interest: None.

1071-9164/$ - see front matter



doi:10.1016/j.cardfail.2007.07.005

center for patients requiring high-intensity tertiary care. The hospital medical records follow the ICD-9 coding system. Hospital medical records from January 2002 to December 2003 were searched using terms ''heart failure,'' ''congestive heart failure,'' ''systolic dysfunction,'' and ''left ventricular dysfunction.'' Patients were included in this study if they met the following criteria for new-onset admitted systolic heart failure: (1) first presentation to the hospital with the diagnosis of congestive heart failure that met the Boston criteria,[4] (2) no prior diagnosis of heart failure or recently diagnosed with systolic heart failure within the last 3 months. Systolic dysfunction was defined as an estimated left ventricular ejection fraction (LVEF) of $< 40\%$ by echocardiography, gated single-photon emission computed tomography imaging or left ventricular angiography. Patients were excluded if (1) LVEF was $\geq 40\%$, (2) there was a prior diagnosis of systolic heart failure dating back $> 3$ months, (3) they had an underlying disease with expected survival $< 6$ months, (4) they had known primary valvular heart disease, whether rheumatic or nonrheumatic, (5) the patient died in-hospital, and (6) no follow-up was available after discharge.

### Data Collection

Hospital charts of 700 patients with a discharge diagnosis of congestive heart failure were screened, of which 220 met inclusion criteria. Reasons for exclusions were as follows: established diagnosis of systolic heart failure (232), heart failure with preserved systolic function (113), malignancy (25), known valvular heart disease (73), and in-hospital death, mostly from comorbid conditions (eg, sepsis with concomitant [often secondary] systolic dysfunction [37]). Complete data were available for 196 patients. Variables recorded included age, sex, history of diabetes mellitus (defined as a fasting glucose $\geq 126$ mg/dL or on treatment), hyperlipidemia (fasting cholesterol $\geq 200$ mg/dL or on treatment), hypertension (systolic blood pressure $\geq 140/90$ mm Hg or on treatment), smoking (ever versus never), prior percutaneous coronary intervention or coronary artery bypass grafting, prior treatment, admission systolic and diastolic blood pressure, pulse, admission laboratory data including white blood cell count, serum creatinine, sodium and hemoglobin, estimate of LVEF by gated single-photon emission computed tomography imaging or left ventricular angiography (if available), QRS width on admission electrocardiogram (estimated manually from the beginning of the first ventricular depolarization to the end of the QRS complex, recorded in milliseconds—a wide QRS was defined as a width $> 120$ ms), and echocardiographic data including dimensions, estimated LVEF, and presence of valvular regurgitation. Echocardiographic data were acquired by experienced technicians as part of routine clinical care. LV dilation was defined as an LV end-diastolic dimension of $> 55$ mm. Hyponatremia was defined as a serum sodium $< 135$ mmol/L. Follow-up information was recorded from the hospital records and then further refined by contacting patients (or family members) by telephone to document out of hospital mortality events or hospitalizations at other institutions. Cardiac mortality was defined as death from documented (or reported) myocardial infarction, heart failure, or sudden death. Sudden cardiac death was defined as recommended by the recent American Heart Association scientific statement.[5] The primary outcome variable was cardiac mortality. The secondary outcome variable was a combination of cardiac death or readmission for congestive heart failure. Only the first hospitalization was considered for this analysis.

### Statistical Methods

All variables were entered into Statistical Package for Social Sciences version 14 (SPSS Inc, Chicago, Illinois, USA). Means and standard deviations were calculated for continuous variables and frequencies for categorical variables. Univariate survival analysis was performed according to the Kaplan-Meier method and differences in survival curves were assessed with the log-rank test. Patients lost at follow-up or dying from noncardiovascular causes were censored at the time of the last visit or contact. Potential survival correlates were further scrutinized with univariate and multivariate Cox proportional hazards models, with calculated risk ratios (HR) for independent variables reported with 95% CI. Variables with a p value of $\leq 0.2$ were entered into the multivariable model. The number of variables considered was intentionally limited because of the relatively small sample size. In a visual evaluation of log(−log(survival)) plots no violation of the proportional hazards assumption became apparent. $P$ values $< .05$ were considered significant. Censored individuals who were lost to follow-up were compared with respect to baseline characteristics to the remaining cohort no significant differences were apparent, thus no violation of the censoring assumptions was noted. Survival curves were plotted using SPSS 14. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

## Results

A total of 196 patients were included in this study. Table 1 shows the baseline characteristics of the study cohort. The mean age was approximately 61 years and with a high preponderance of males. This was a relatively unhealthy group of patients with more than 60% suffering from hypertension and diabetes mellitus and more than three-fourths having a history of coronary artery disease in the past. Mean ejection fraction was 25% and, consistent with the selection of new-onset cases, only a minority were on renin-angiotensin blocking agents (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker) before admission. Surprisingly, despite a previous history of coronary artery disease, only 13% were on β-blockers before presentation.

The median (interquartile range) follow-up time was 379 (211 to 500) days, respectively. After discharge from the hospital, a high event rate was observed in this cohort. A total of 54 patients (27.5%) died, of which 50 (92.5%) were cardiovascular in origin. Of these, at least 12 (22.2%) died suddenly. Seventy-three patients (37.2%) required rehospitalization for congestive heart failure. The combined event (death or hospitalization for heart failure) occurred in 102 patients (52%) over this follow-up period (median event-free survival of 324 days).

Figure 1 shows the Kaplan-Meier curves for the overall survival experience of the cohort in terms of the primary and combined endpoints. As can be seen, there is a steady increase in the cumulative incidence of events with time.

Table 2 shows the univariate predictors of mortality in our cohort. On univariate analysis, admission pulse, systolic blood pressure, serum sodium, and β-blockers at discharge were significantly associated with mortality. Trends of

**Table 1.** Baseline Characteristics of Patients with New-Onset Systolic Heart Failure Admitted to a Tertiary Care Hospital in Pakistan (n = 196)

| Baseline Characteristics | n |
|---|---|
| Age (mean [SD]) | 61.2 (12.8) |
| Male | 127 (64.8) |
| Signs and symptoms | |
| Dyspnea at rest | 177 (90.3) |
| Orthopnea | 145 (74.0) |
| Dyspnea on mild exertion | 19 (9.7) |
| Pulse (mean [SD]) | 97 (22) |
| Pulse >100/min | 73 (37.2) |
| SBP (mean [SD]) mm Hg | 131.9 (30.1) |
| DBP (mean [SD]) mm Hg | 79.3 (19.0) |
| SBP <100 mm Hg | 28 (14.4) |
| Mean arteria pressure (mean [SD]) mm Hg | 96.9 (21.3) |
| Jugular venous distension | 112 (57.1) |
| Rales on examination | 164 (83.7) |
| Third heart sound | 42 (21.4) |
| Pedal edema | 14 (7.1) |
| Pulmonary edema on chest radiograph | 179 (91.3) |
| Hypertension | 132 (67.3) |
| Diabetes mellitus | 119 (60.7) |
| Smoking | 59 (30.1) |
| Prior CAD* | 150 (76.5) |
| Hyperlipidemia | 81 (41.3) |
| Prior ACEI/ARB therapy | 15 (7.7) |
| Prior β-blocker therapy | 25 (12.8) |
| Troponin elevation† | 46 (27.7) |
| EF (mean [SD]) | 25 (8.6) |
| Dilated LV‡ | 77 (43.8) |
| Severe mitral regurgitation | 60 (30.6) |
| Creatinine (mean [SD]) mg/dL | 1.7 (1.4) |
| QRS wide (> 120 ms) | 35 (19.3) |
| Serum sodium (mean [SD]) mmol/L | 133.9 (6.4) |
| Hyponatremia§ | 98 (50.0) |
| Discharge medications | |
| ACEI or ARB | 164 (83.7) |
| β-blockers | 118 (60.2) |
| Aspirin | 160 (81.6) |

Parentheses indicate percentages unless otherwise stated. SD, standard deviation; SBP, systolic blood pressure; CAD, coronary artery disease; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; EF, ejection fraction; LV, left ventricle.

*Defined as prior history of documented infarction, ischemia on stress test, or disease on angiography.

†Defined as >1.0 ng/mL.

‡Defined as left ventricular end diastolic dimension >55 mm; missing data in 20 patients.

§Na <135 mmol/L.

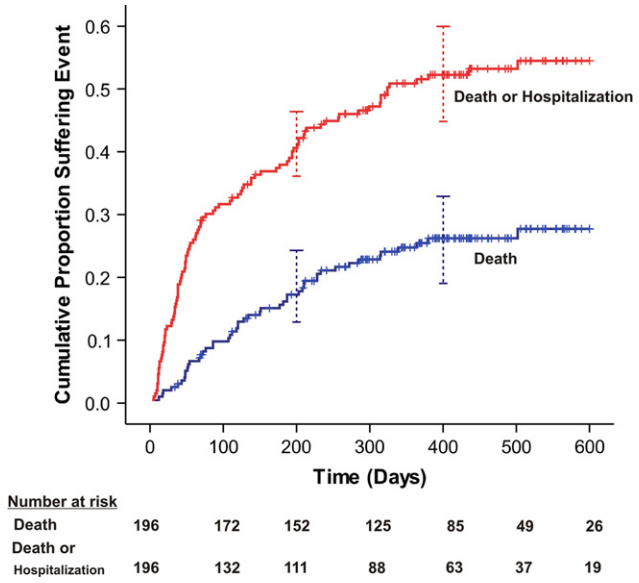


**Fig. 1.** Cumulative incidence of death and combined end point of death or hospitalization for heart failure in patients with new onset systolic heart failure admitted to a tertiary care hospital in Pakistan (n = 196). Ticks on cumulative incidence curves represent censored events. Vertical bars represent 95% confidence limits of the estimated proportion suffering end points at time intervals of 200 and 400 days in each curve.

association with mortality were noted with severe mitral regurgitation (versus no severe regurgitation), low pulse pressure (<40 mm Hg), anemia (hemoglobin <10 g/dL), and elevation of serum troponin. On Cox proportional hazards multivariate regression (Table 3), serum sodium, admission systolic blood pressure, pulse on admission, and severe mitral regurgitation were significantly associated with mortality after discharge. The only independent predictor for the combined end point was discharge on renin-angiotensin blocking agents (HR 0.60 [95% CI 0.37−0.97]; $P = .037$).

## Discussion

This is the first study from the Indo-Pakistan subcontinent, home to one-sixth of the world's population, describing the patient characteristics and clinical outcomes of patients requiring admission for systolic heart failure. We describe a high mortality and morbidity over a median follow-up of less than 1 year with nearly a quarter dying and more than half experiencing the combined end point of death or hospitalization for heart failure. Independent correlates of mortality in our cohort included serum sodium, systolic blood pressure, and pulse on admission and severe mitral regurgitation on echocardiography.

There are several possible reasons for the high mortality and morbidity noted in our study. First, as seen in Table 1, the study group is a fairly unhealthy population with a majority suffering from diabetes mellitus, hypertension, and previous coronary artery disease. Second, by design, our study looked at patients with systolic dysfunction who required admission. This group of heart failure patients is inherently high risk. Earlier studies suggested a very high mortality of hospitalized heart failure.[6,7] These studies were published in the days prior to routine initiation of angiotensin-converting enzyme inhibitor therapy in heart failure. More recently, Roguin and colleagues[8] described a nearly 40% 1-year mortality in patients discharged after acute heart failure. Shahar and colleagues analyzed a large database of heart failure admissions spanning more than 22 hospitals and reported a 1-year mortality of more than 30%.[9] Almost identically, Lee et al reported a 32.9% a 1-year mortality in more than 4000 community-based Canadian patients admitted for heart failure.[10] These studies were more heterogenous in that they included patients with prior diagnoses of heart failure, many of whom were

**Table 2.** Univariate Predictors of Survival in Patients Admitted With New-Onset Systolic Heart Failure at a Tertiary Care Hospital in Pakistan (n = 196)

| | Survived (n = 146) | Died (n = 50) | Unadjusted HR (95% CI) | *P* Value |
|---|---|---|---|---|
| Age (mean [SD]) | 61.3 (11.7) | 60.8 (15.7) | 1.00 (0.97−1.02) | .681 |
| Male sex | 97 (66.4) | 30 (60.0) | 1.00 (0.97−1.02) | .681 |
| Diabetes mellitus | 89 (61.0) | 30 (60.0) | 0.96 (0.54−1.69) | .880 |
| Hypertension | 101 (69.2) | 31 (62.0) | 0.73 (0.41−1.30) | .287 |
| Smoking | 47 (32.2) | 12 (24.0) | 0.67 (0.35−1.30) | .234 |
| Troponin elevation[§] | 31 (24.6) | 15 (37.5) | 1.71 (0.90−3.24) | .103 |
| EF (mean [SD]) | 24.9 (8.4) | 22.9 (8.3) | 0.97 (0.94−1.01) | .141 |
| LV dilation[§] | 56 (43.4) | 21 (47.0) | 1.00 (0.56−1.78) | .996 |
| Severe MR* | 40 (27.4) | 20 (40.0) | 1.70 (0.97−3.00) | .066 |
| Diastolic dysfunction | 91 (62.3) | 33 (66.0) | 1.16 (0.65−2.10) | .617 |
| Renal insufficiency[‡] | 44 (30.1) | 14 (28.0) | 0.97 (0.52−1.83) | .934 |
| PASP (mean [SD]) | 50.5 (13.1) | 51.4 (14.0) | 1.01 (0.98−1.04) | .545 |
| QRS wide (>120 ms) | 25 (17.1) | 10 (20.0) | 1.14 (0.57−2.30) | .715 |
| Hemoglobin (mean [SD]) g/dL | 12.3 (2.0) | 12.1 (2.1) | 0.94 (0.83−1.08) | .397 |
| Anemia (Hb < 10 g/dL) | 19 (13.3) | 9 (18.0) | 1.52 (0.74−3.12) | .259 |
| SBP (mean [SD]) mm Hg | 134.9 (30.9) | 122.8 (25.8) | 0.98 (0.97−0.99) | .008 |
| SBP < 100 mm Hg | 17 (11.6) | 11 (22.0) | 2.05 (1.05−4.01) | .037 |
| Low pulse pressure (<40 mm Hg) | 24 (16.6) | 13 (26.0) | 1.74 (0.92−3.27) | .089 |
| Pulse (mean [SD]) beats/min | 95.4 (21.6) | 103 (22.7) | 1.01 (1.00−1.02) | .042 |
| Pulse >100/min | 48 (32.9) | 25 (50.0) | 1.82 (1.04−3.16) | .035 |
| Sodium (mean [SD]) mmol/L | 134.8 (5.7) | 131.1 (7.5) | 0.93 (0.90−0.97) | <.001 |
| Hyponatremia (<135 mmol/L) | 65 (44.5) | 33 (60.0) | 2.28 (1.27−4.11) | .005 |
| β-blockers at discharge | 95 (65.1) | 23 (46.0) | 0.49 (0.28−0.85) | .012 |
| ACEI/ARB at discharge | 124 (84.9) | 40 (80.0) | 0.66 (0.33−1.32) | .233 |
| Ischemic CMP[†] | 110 (75.3) | 41 (80.0) | 1.26 (0.63−2.51) | .511 |

Parentheses in first two columns indicate percentages unless otherwise stated. HR, hazards ratio; CI, confidence interval; SD, standard deviation; CAD, coronary artery disease; ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; EF, ejection fraction; LV, left ventricular; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; Hb, hemoglobin; Hg, mercury; CMP, cardiomyopathy.

*Versus no severe MR.

[‡]Creatinine >1.5 mg/dL.

[†]Defined as history of prior documented MI, prior coronary revascularization (coronary artery bypass graft or percutaneous coronary intervention) or known CAD by prior angiography or positive functional study (echocardiographic or nuclear) or elevation of cardiac troponin during present admission >1 ng/mL.

[§]Missing data.

already on angiotensin-converting enzyme inhibitors/angiotensin receptor blockers or β-blocker therapy; therefore, their hospitalization represents failure of therapy (and thus higher risk). However, a recent population-based study by Cowie et al in patients with new heart failure referred from general practitioner offices for acute admission had a dismal prognosis: the 1-year survival rate was only 62%. Our study limited itself to new-onset systolic heart failure and also reports a high mortality in the first year after discharge, emphasizing that hospitalization for systolic heart failure marks a highly adverse prognosis. Third, ours being a referral center may have attracted high-risk patients, leading to the high event rate. Our selection of new cases would be expected to reduce the effect of this bias. However, it is also possible that many of the so called ''new-onset'' failure patients were simply patients with an established (but undiagnosed) problem who eventually presented to the hospital when their conditioned worsened. Thus paradoxically, they may have been high-risk subjects.

Our findings of a strong association between serum sodium, systolic blood pressure, and pulse with mortality are consistent with reported data, including the Heart Failure Survival Score and Seattle Heart Failure Model[11,12] as well as a recent Canadian study in which patients had very similar characteristics.[10] Hyponatremia is a marker of neurohormonal activation, particularly rennin, and has consistently been associated with adverse outcomes.[13] Tachycardia reflects activation of the sympathetic neurohormonal system and is also associated with poor outcomes.[14] Likewise, low blood pressure inherently reflects severity of disease and, not surprisingly, has been associated with

**Table 3.** Cox Proportional Hazards Model Showing Multivariate Predictors of Mortality in Patients Admitted With New-Onset Systolic Heart Failure at a Tertiary Care Hospital in Pakistan (n = 196)

| | Adjusted HR (95% CI)* | *P* Value |
|---|---|---|
| Sodium[†] | 0.94 (0.90−0.97)[‡] | <.001 |
| SBP[†] | 0.98 (0.97−0.99)[‡] | .016 |
| Pulse[†] | 1.02 (1.01−1.04)[‡] | .002 |
| Severe MR[§] | 1.90 (1.03−3.48) | .039 |

Cox model $\chi^2$ 33.7; df = 4.

HR, hazards ratio; CI, confidence interval; SBP, systolic blood pressure; Hg, mercury; MR, mitral regurgitation.

*Adjusted for smoking, beta blockers at discharge, angiotensin converting enzyme inhibitor/angiotensin receptor blocker at discharge, anemia, troponin elevation, and ejection fraction. HR (95% CI) using categorical cut points as follows: sodium <135 mmol/L, 2.39 (1.30−4.37); SBP <100 mm Hg, 2.13 (1.07−4.24); pulse >100/min, 2.28 (1.27−4.08).

[†]As recorded on admission.

[‡]For each unit increase.

[§]Versus no severe MR.

worse outcomes in other studies also.[15] Consistent with these findings, β-blockers at discharge was noted to be protective against mortality on univariate analysis. We found a relatively high prevalence of severe mitral regurgitation (30.6%) in our cohort, in line with other data.[16] This independent relationship of severe mitral regurgitation with mortality has also been reported elsewhere.[17]

Our study did not show an independent relationship with mortality for some factors that deserve mention. LVEF has been shown to be a strong predictor of mortality in general with a significant reduction in survival as the LVEF declines from the highest to the lowest quartile. We did not see such a relationship in our study. One possible reason is that the LVEF range was fairly narrow (median LVEF 20%, interquartile range 20 to 30), and sample size limitations may not have allowed a relationship between LVEF and mortality to surface. More important, New York Heart Association class is a far more robust predictor of outcome[18] and it is possible that the effect of requiring hospitalization superseded the differential prognosis that LVEF may otherwise confer on patients. Clinical trials have shown that in general, symptomatic patients have modestly lower LVEFs than asymptomatic patients yet the prognosis of the former is much worse.[19,20] Thus the lack of a relationship between LVEF and mortality in this patient subset is not entirely surprising. QRS prolongation has been reported in some series as a predictor of mortality.[21] However, our data did not suggest any difference in outcome between those with normal and wide QRS complex at presentation. Diastolic dysfunction, in particular a restrictive mitral inflow pattern is associated with higher cardiac mortality in heart failure.[22] We saw a trend supporting this association but in the multivariable analysis this was not an independent predictor, possibly from sample size limitations. Heart failure from ischemic heart disease tends to have a worse prognosis than nonischemic cardiomyopathy.[23] That ischemic heart was the predominant mechanism of heart failure in the majority of our patients may have prevented such a relationship from becoming evident.

Our study is not without limitations. First, this is a single-center experience and our results may not be extrapolated to the entire Pakistani population. However, our hospital caters to a wide mix of patients, ranging from affluent to poor, somewhat reflective of the population at large. Second, as discussed previously, ours being a tertiary care center may have potentially attracted patients with identifiable (and covert) adverse prognostic features, leading to the observed high mortality. However, we recruited patients with new-onset heart failure in the hope to avoid such bias. Of course we cannot distinguish between those patients with truly new-onset disease and those with undiagnosed heart failure that led to an admission when the condition worsened. Third, we did not incorporate the effect of revascularization into our predictive model. However, owing to cost limitations, the majority of patients in this cohort did not undergo revascularization. Fourth, the effect of compliance to medical therapy was not assessed in this study. Finally, because of the retrospective nature of the study several important variables are missing in our study including reliable documentation of signs and symptoms as well as anthropometric values. Furthermore, we also do not have outcomes data on patients admitted for heart failure with preserved systolic function. We are therefore unable to comment on any relationship between outcomes and variables such as obesity in this cohort nor are we able to compare outcomes of hospitalized heart failure in those with low versus preserved systolic function.

In conclusion, this is the first report from the Indo-Pakistan subcontinent on outcomes of patients suffering from systolic heart failure requiring admission. We report a high 1-year mortality and an even higher combined event rate (death or hospitalization for heart failure) emphasizing the highly adverse prognosis of the disease. The number of patients with systolic heart failure is bound to rise as the burden of cardiovascular disease in the region continues to soar. Therefore measures to prevent ischemic heart disease and its lethal sequelae are essential as developing nations simply cannot afford to treat and manage heart failure with their meager health care resources. Further study is warranted to determine whether the prognosis of Indo-Asian patients admitted with heart failure but have preserved systolic function is similarly adverse.

## References


1. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol 1993;22:6A.
2. Levy D, Kenchaiah S, Larson MG, et al. Long-term trends in the incidence of and survival with heart failure. N Engl J Med 2002;347:1397.
3. Krumholz HM, Parent EM, Tu N, et al. Readmission after hospitalization for congestive heart failure among Medicare beneficiaries. Arch Intern Med 1997;157:99.
4. Marantz PR, Tobin JN, Wassertheil-Smoller S, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. Circulation 1988;77:607.
5. Luepke RV, Apple FS, Christenson RH, et al. Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. Circulation 2003;108:2543.
6. Clark LT, Garfein OB, Dwyer EM Jr. Acute pulmonary edema due to ischemic heart disease without accompanying myocardial infarction. Natural history and clinical profile. Am J Med 1983;75:332.
7. Wiener RS, Moses HW, Richeson JF, Gatewood RP Jr. Hospital and long-term survival of patients with acute pulmonary edema associated with coronary artery disease. Am J Cardiol 1987;60:33.
8. Roguin A, Behar D, Ben Ami H, et al. Long-term prognosis of acute pulmonary oedema—an ominous outcome. Eur J Heart Fail 2000;2:137.
9. Shahar E, Lee S, Kim J, Duval S, Barber C, Luepker RV. Hospitalized heart failure: rates and long-term mortality. J Card Fail 2004;10:374.

10. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA 2003;290:2581.
11. Levy WC, Mozaffarian D, Linker DT, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. Circulation 2006;113: 1424.
12. Aaronson KD, Schwartz JS, Chen TM, Wong KL, Goin JE, Mancini DM. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. Circulation 1997;95:2660.
13. Lee WH, Packer M. Prognostic importance of serum sodium concentration and its modification by converting-enzyme inhibition in patients with severe chronic heart failure. Circulation 1986;73: 257.
14. Lechat P, Hulot JS, Escolano S, et al. Heart rate and cardiac rhythm relationships with bisoprolol benefit in chronic heart failure in CIBIS II Trial. Circulation 2001;103:1428.
15. Lee TT, Chen J, Cohen DJ, Tsao L. The association between blood pressure and mortality in patients with heart failure. Am Heart J 2006;151:76.
16. Patel JB, Borgeson DD, Barnes ME, Rihal CS, Daly RC, Redfield MM. Mitral regurgitation in patients with advanced systolic heart failure. J Card Fail 2004;10:285.
17. Koelling TM, Aaronson KD, Cody RJ, Bach DS, Armstrong WF. Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. Am Heart J 2002;144:524.
18. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). The CONSENSUS Trial Study Group. N Engl J Med 1987;316:1429.
19. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigators. N Engl J Med 1992;327:685.
20. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators. N Engl J Med 1991;325:293.
21. Iuliano S, Fisher SG, Karasik PE, Fletcher RD, Singh SN. QRS duration and mortality in patients with congestive heart failure. Am Heart J 2002;143:1085.
22. Xie GY, Berk MR, Smith MD, Gurley JC, DeMaria AN. Prognostic value of Doppler transmitral flow patterns in patients with congestive heart failure. J Am Coll Cardiol 1994;24:132.
23. Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. N Engl J Med 2000;342:1077.