

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.

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

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doi:10.1016/j.cardfail.2007.07.005

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

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 ≥ 126 mg/dL or on treatment), hyperlipidemia (fasting cholesterol ≥ 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 ≤ 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 $\log(-\log(\text{survival}))$ 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

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