To determine which of the many clinical parameters routinely collected influence mortality in patients with congestive heart failure (CHF), 201 patients with idiopathic or ischemic dilated cardiomyopathy were prospectively followed for a 28-month study period. Mean age of the study group was 62 +/- 10 years, 60% had ischemic cardiomyopathy, and two-thirds were in New York Heart Association functional class II or III. Fifteen clinical variables were analyzed using a Cox proportional hazards model, while individual variables also were calculated for independent prognostic significance. There were 85 deaths, 26 (31%) of which were sudden cardiac deaths. Three characteristics at the study entry independently predicted an increased mortality risk: left ventricular ejection fraction, maximal oxygen uptake and ischemic cardiomyopathy. A Cox proportional hazards model showed that the combination of VO2max, S3 and the diagnosis of ischemic cardiomyopathy provided the best estimates of risk for an early death. Mortality for the low-risk group was only 5% at 6 months and 10% at 1 year. In contrast, in patients with an S3, ischemic cardiomyopathy and low maximal oxygen uptake, 6-month mortality was 24% and 36% at 1 year (p less than 0.001). Thus, these patients at high risk with left ventricular dysfunction associated with ischemic heart disease, a decreasing exercise tolerance and the development of an S3 should be strongly considered for an interventional trial with the aim of decreasing mortality.