OBJECTIVES: This study sought to assess proinflammatory cytokine levels in patients in the studies of left ventricular dysfunction trial (SOLVD) in relation to both their New York Heart Association functional classification and their neurohormonal status before randomization.

BACKGROUND: Elevated levels of tumor necrosis factor-alpha have been identified in 30% to 40% of patients with heart failure. However, it is unclear which subsets of patients with heart failure elaborate tumor necrosis factor-alpha. It is also unclear what the mechanism for the increased expression of proinflammatory cytokines is.

METHODS: Tumor necrosis factor-alpha and interleukin-6 levels were analyzed by enzymes-linked immunoassay using randomly selected plasma samples from patients in functional classes I to III who were enrolled in neurohormonal substudies of the SOLVD trial; age-matched healthy subjects served as the control group.

RESULTS: Plasma levels of tumor necrosis factor-alpha (p < 0.001) were elevated in patients in functional classes I to III ([mean +/- SD] 1.95 +/- 0.54, 2.63 +/- 0.48, 6.4 +/- 1.9 pg/ml, respectively) compared with age-matched control subjects (0.75 +/- 0.05 pg/ml) and were progressively elevated in relation to decreasing functional status of the patient. Plasma levels of interleukin-6 (p < 0.001) were elevated in patients in functional classes I to III (3.3 +/- 0.55, 6.2 +/- 1.1, 5.22 +/- 0.9 pg/ml, respectively) compared with age-matched control subjects (1.8 +/- 0.5 pg/ml and were progressively elevated in relation to decreasing functional status of the patient. Cox proportional-hazards analysis showed that there was a trend toward significance between plasma tumor necrosis factor-alpha (p < 0.07) and survival, whereas there was no significant relation for plasma interleukin-6 (p < 0.72). Except for atrial natriuretic factor, which correlated weakly (r = 0.23, p = 0.04) with circulating tumor necrosis factor-alpha levels, there was no significance correlation between neurohormonal and proinflammatory cytokine levels.

CONCLUSIONS: Circulating levels of proinflammatory cytokines increase in patients as their functional heart failure classification deteriorates. Moreover, activation of the neurohumoral axis is unlikely to completely explain the elaboration of proinflammatory cytokines in heart failure.