

**Depression as an independent risk factor for all-cause mortality in heart failure patients**

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**Topic(s):**

Co-morbidities

**Citation:**

European Journal of Heart Failure Abstracts Supplement ( 2015 ) 17 ( Supplement 1 ), 69

**Purpose:** Depression is reported to be associated with mortality among patients with heart failure (HF). However, whether this reflects more severe disease or a greater co-morbidity or is independent of such risk factors is unclear.

**Methods:** OPERA-HF is an observational study enrolling patients hospitalized with heart failure. Inclusion criteria were: age > 18 years, hospitalized for or with HF and treated with loop diuretics and at least one of the following: left ventricular ejection fraction  $\leq 40\%$ , left atrial dimension > 4.0 cm or NT-ProBNP >400 pg/ml (if in sinus rhythm) or > 1200 pg/ml (if in atrial fibrillation)). Depression was assessed by Hospital Anxiety and Depression Scale (HADS-D) questionnaire. Co-morbidity was assessed by the Charlson Comorbidity Index (CCI). Kaplan-Meier and Cox regression analyses were used to estimate the association between depression and all-cause mortality.

**Results:** Of 154 patients that completed the HADS-D questionnaire, 103, 27 and 24 patients had no-to-normal (score 0-7), mild (score 8-10) or moderate-to-severe (score 11-21) depression, respectively. Over a mean follow-up time of 302 days, 27 out of 154 patients died. In univariate Cox regression analysis, moderate-to-severe depression was associated with an increased risk of death (HR: 5.11; 95% CI: 2.39 to 10.93;  $P < 0.001$ ) comparing to no-to-normal or mild depression. Moderate-to-severe depression remained a significant predictor of mortality after controlling for sex, age, hypertension and NT-proBNP (HR: 6.50; 95% CI: 2.19 to 19.32;  $P < 0.001$ ); and changed little with the further inclusion of the CCI in the model (HR: 5.38; 95% CI: 1.84 to 15.67;  $P < 0.005$ ). On the other hand, a low HADS-D score between 0 and 7 was associated with a decreased mortality risk (HR: 0.21; 95% CI: 0.09 to 0.46;  $P < 0.001$ ).

**Conclusion:** This analysis suggests that depression is strongly associated with an adverse outcome in the year after discharge from a HF hospital episode and that it may not be explained by the severity of HF or co-morbidity. Recognition and management of depression might improve outcome. Appropriately designed randomized trials are required.