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

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Purpose

Psychosocial factors such as depression are often associated with worsening outcomes in patients with cardiovascular disease. [Ladwig et al.]
In patients with heart failure (HF), depression is 4–5 times more prevalent than in the general population [Parissis et al.] and is often reported to be associated with increased mortality.
However, it is unclear whether depression is independently related to mortality or simply reflects more severe HF and/or co-morbidities.

Methods

OPERA-HF study outline

An ongoing observational study enrolling patients hospitalized with HF to the Hull & East Yorkshire Hospitals NHS Trust.
Clinical and psycho-social data were collected during hospital admission and just prior to discharge.

Inclusion criteria
Age > 18 years, hospitalized for or with HF and treated with loop diuretics and at least one of the following: left ventricular ejection fraction ≤ 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)).

Exclusion criteria
Unable to understand and comply with the protocol or to give informed consent.

Measurements

- *Hypertension* recorded at enrollment
- *NT-proBNP* measured at discharge
- Co-morbidity assessed by *Charlson Comorbidity Index (CCI)* (Charlson et al. (1987)). CCI is calculated during hospitalization by assigning to certain comorbidities a weighted value.
- Depression assessed at enrollment by *Hospital Anxiety and Depression Scale (HADS-D)* questionnaire (Zigmond and Snaith (1983)). Only questionnaire items that relate to depression were used. Partial scores are added up to determine the depression score which ranges from 0 to 21. A score of 7 or less is found to reflect an absence of depression, a score of 8-10 reflects mild depression and a score of 11 or more moderate-to-severe depression.

Results

- **301 HF patients are currently enrolled in the study.**
- **Results based on 154 HF patients who completed the HADS-D questionnaire.**
- **One year incidence rate (all-cause mortality) = 17.7%**

Table 1: Number of patients and characteristics per HADS-D group

Depression level	None		Mild		Moderate-to-severe		All	
Score	[0-7]		[8-10]		[11-21]		[0-21]	
Total number of patients	103		27		24		154	
Number of Deaths	9 (8.7%)		6 (22.2%)		12 (50%)		27 (17.5%)	
Characteristics	Valid N	N (%) Median [25th – 75th]	Valid N	N (%) Median [25th – 75th]	Valid N	N (%) Median [25th – 75th]	Valid N	N (%) Median [25th – 75th]
Women, %	103	28.2%	27	33.3%	24	29.2%	154	29.2%
Age, y	102	72 [65 – 81]	27	70 [65.5 – 74.5]	24	70 [61.75 – 78.5]	153	71 [64 – 79]
Hypertension, %	99	53.5%	26	53.8%	21	71.4%	146	56.2%
NT-proBNP, pg/ml	86	5240 [1918 – 10400]	21	3779 [1375 – 11830]	20	6110 [2812 – 12640]	127	5097 [1889 – 11070]
CCI, score	97	2 [2 – 4]	23	4 [2.5 – 7]	22	3 [1.25 – 5.75]	142	3 [2 – 5]

Figure 1: Unadjusted survival curve

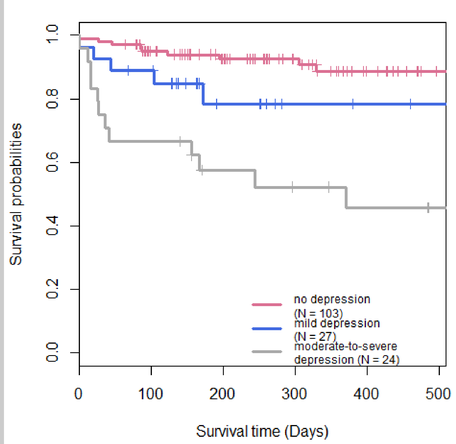

Figure 2: Adjusted survival curve

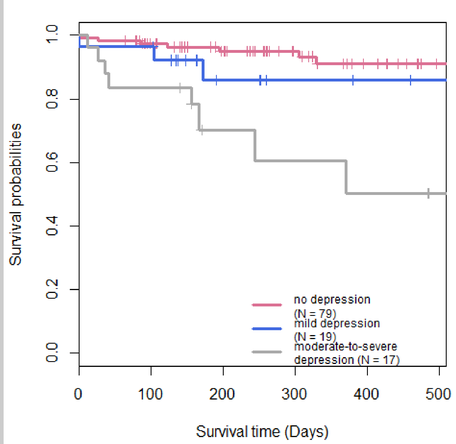

Table 2: Univariate and multivariate analysis [all-cause mortality outcome]

	Univariate (N = 154)		Mulivariate* (N = 115)	
Depression Status	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
None (reference)	1	-	1	-
Mild	2.99 (1.07 - 8.45)	< 0.05	2.93 (0.84 - 10.20)	< 0.1
Moderate-to-severe	6.97 (2.93 - 16.56)	< 0.001	6.96 (2.19 - 22.15)	< 0.01

* controlling for sex, age, hypertension, NT-proBNP and CCI

Statistical analysis

Univariate and multivariate Cox proportional hazard regression model were used to estimate the association between depression and all-cause mortality.

In the multivariate models moderate-to-severe depression was adjusted for:
- Sex (female)
- Age (continuous)
- Hypertension (yes)
- NT-proBNP (continuous)
- CCI (continuous)

Kaplan-Meier method used to estimate survival time and produce a survival curve.

All analysis was conducted using R statistical software (version 3.1.3).

Conclusion

Depression is strongly associated with an adverse outcome following hospital discharge for patients admitted with HF; this does not just appear to be due to the severity of HF or physical co-morbidity. Recognition and management of depression might improve patient outcomes. However, due the limited number of observed events a larger study is required to confirm our results.

References

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Declaration of interest

IS, JJGV, JMR, SCP, GG and AT are employed by Philips Research. ACG, KMG, JGC and ALC have received departmental research support from Philips.