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Incidence rates and predictors of major and minor depression in patients with heart failure☆

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ABSTRACT

Aims: Depression is common in heart failure (HF) and associated with adverse outcomes. This study aimed to investigate incidence rates and predictors of depression in patients sampled from four subprojects of the German Competence Network Heart Failure.
Methods: Eight hundred thirty nine symptomatic HF patients free of depression at baseline underwent repeat depression screening (Patient Health Questionnaire, PHQ-9) after 12 months. Ordered logistic regression analysis was employed to search for predictors of incident depression.
Results: Incident minor (major) depression was observed in 61 (7.3%) and 47 (5.6%) of the population. Depression was recurrent in 15 (25%) and 16 (34%), respectively. Multiple regression analysis revealed seven variables predicting minor or major depression: Previous depressive episode (odds ratio [OR] 4.04, 95% confidence interval [CI] 2.37–6.89, $p \leq 0.001$), previous resuscitation (OR 2.44, CI 1.23–4.81, $p = 0.010$), current smoking (OR 2.06, CI 1.08–3.50, $p = 0.008$), >4 visits/year to general practitioner (OR 1.67, CI 1.06–2.63, $p = 0.026$), New York Heart Association class (OR 1.54/class, 95% CI 1.05–2.25, $p = 0.027$), PHQ-9 baseline sum-score (OR 1.18/point, CI 1.11–1.27, $p < 0.001$), and SF-36 physical functioning (OR 1.08/−5 points, CI 1.03–1.13, $p = 0.002$).
Conclusions: In these HF patients initially free of depression annual incidence rates were high. Several independent predictors allowed identification of patients at particular risk. Although obtained in a selected cohort these findings call, in view of the grave prognosis of HF patients with comorbid depression, for regular depression screening and development of specific supportive strategies to improve patient care and outcomes in HF.

1. Introduction

Depression is common in patients with heart failure (HF). Prevalence rates range from 11 to 25% in outpatients and 35 to 70% in hospitalised patients [1]. Co-morbid depressive disorder is a predictor of mortality, rehospitalisation and worsening HF [2,3], but still remains often unappreciated in routine patient care [4,5]. In view of its prognostic relevance the American Heart Association recently published the recommendation to screen all patients post myocardial infarction for depression [6]. However, depression treatment with medication or psychotherapy has so far not been shown to improve outcomes

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in cardiovascular patients, and was associated with only modest and inconsistent improvement in depressive symptoms [7].

Previous cross-sectional studies identified various conditions frequently complicating HF as anaemia, diabetes mellitus, systemic inflammation or obstructive pulmonary disease [8,9], NYHA functional class, history of depression or female sex [1,5,8,9] as correlates of co-morbid depressive disorder, and HF emerged as an independent risk factor for incident depression in a large population-based cohort [10]. Further, recent reports suggest that increasing depressive symptoms may worsen [11], and remission from depression improve cardiovascular outcomes [12]. Regarding predictors of depression in HF evidence relies to our knowledge on one relatively small study investigating a restricted number of variables [13,14]. Probably as a consequence of limited sample size risk factors for major and minor depression were not investigated separately in this study, and gender aspects were not considered.

The development of preventive strategies requires comprehensive knowledge of predisposing factors and early recognition of HF patients at risk for depressive disorders. The aims of the current study were, therefore, to define incidence rates of minor as well as major depression in a large cohort of well characterised patients with established systolic HF, to ascertain in this population predictors for minor as well as major depression from a wide spectrum of demographic, clinical and laboratory variables considering also possible gender differences, and to elaborate implications for patient management.

2. Materials and methods

2.1. Study flow and subjects

Funded by the German Federal Ministry for Education and Research, the CNHF provides an organisational structure to network high-quality patient-oriented research in HF. To facilitate data analyses across different studies, the same comprehensive basic clinical dataset (BCD) is prospectively acquired in all CNHF subprojects [15]. Patients qualified for the present analysis if recruited into one of four CNHF projects with prospectively scheduled re-assessment after 12 months, and if not undergoing any interventions potentially impacting on patients' state of mood (CNHF subprojects 9a, 10, 13 15) [15]. Further participation criteria comprised a) acquisition of the complete BCD both at baseline and after 12 months, including also psychometric evaluation with the Patient Health Questionnaire 9-item depression module (PHQ-9) [16] and the 36 item Short Form Health Survey (SF-36) [17]; b) symptomatic chronic systolic HF (New York functional class II-IV) with a left ventricular ejection fraction (LVEF) of 45% or less at the time of inclusion; c) absence of any current depressive disorder at baseline according to the PHQ-9 categorical evaluation.

2.2. Basic clinical data set

2.2.1. Demographics and clinical assessment

Study participants underwent standardised clinical work-up including detailed a history including medication, physical examination, laboratory assessment, 12-lead electrocardiogram, and echocardiography. The following definitions were applied: Peripheral oedema, palpable swelling of soft tissues in ankles or lower legs due to fluid accumulation; hypertension, sitting blood pressure >140/90 mmHg or history of hypertension before introduction of medications for hypertension or HF; chronic obstructive pulmonary disease (COPD), history of COPD requiring bronchial treatment or pulmonary obstruction newly diagnosed by function testing. For further definitions see Table 1. Left ventricular ejection fraction (LVEF) was measured from two-dimensional echocardiograms using the biplane or single plane Simpson method.

2.2.2. Psychometric evaluation

Depression was assessed using the German PHQ-9-version [18]. Each item corresponds to one of nine DSM-IV diagnostic A-criteria for major depressive disorder [19]. In accordance with Loewe and coworkers [18], a minor (major) depressive episode was assumed if 2–4 (≥5) of the 9 items were present on "more than half the days" and one item was depressed mood or anhedonia. The last item (suicidal ideation, ideas of self-harm) contributed to establishing the diagnosis, if present at all. Physical functioning and bodily pain scales as derived from the SF-36 were employed to characterise the degree of subjective physical impairment and suffering from pain [17].

2.3. Data analysis

Data are presented as frequencies and percentages for binary, and mean and standard deviation for quantitative variables. Kendall's rank correlation test was employed to examine the relationship of each baseline variable with incident minor or major depression. Multiple ordinal logistic regression analysis was performed to identify independent predictors. *P*-values ≤0.05 were considered significant. Using the final regression model, probabilities of incident minor and major depression were assessed in all eligible patients. The predicted incidence rates of patients who did, and those who did not provide follow-up PHQ-9 were compared in order to examine possible selection bias.

3. Results

3.1. Subjects

At baseline, 1175 patients met the inclusion criteria. However, at follow-up after 12 months 109 patients (9.3%) had died, 69 (5.9%) chose not to complete another PHQ-9 questionnaire, and 158 (13.4%) were lost to follow-up. Thus, 839 subjects (62.5 ± 12.6 years, 76.6% males) were eligible for analysis. Baseline characteristics are given in Table 1. Coronary artery disease was the leading cause of HF, followed by dilated cardiomyopathy and various other diseases. Most patients had mild HF at baseline. Patients exhibiting depression after 12 months were more often in NYHA classes III and IV, and 9.4% reported at least one previous depressive episode.

3.2. Depression incidence rates

There were 61 (7.3%) cases of incident minor and 47 (5.6%) of incident major depression. Thus, the overall incidence rate was 12.9% (95% CI: 10.6 to 15.2%) or 129 new cases in 1000 person-years. Fifteen (25%) of the minor and 16 (34%) of the major depression episodes were recurrent amounting to an overall depression recurrence rate 3.7% or 37 cases per 1000 person-years.

3.3. Predictors of incident major and minor depression

Table 1 also lists Kendall's tau rank correlation test results describing the relationship between PHQ-9 sum scores and patients' baseline characteristics. In univariate analysis, several demographic variables (female gender, living alone), indicators of perceived disease severity (NYHA class, number of visits to general practitioner), quality of heart failure pharmacotherapy as assessed by the global adherence indicator 3 (GAI 3) [20], interventions (percutaneous coronary revascularisation, resuscitation) during follow up, risk factors and co-morbidities (current smoking, hyponatraemia, renal dysfunction) and measures of quality of life and depression correlated with incident depression, while alcohol consumption and use of cardiac glycosides were inversely correlated. Remarkably, objective markers of cardiovascular status as LVEF, HF etiology, the presence of oedema, heart rate and pulse pressure were not correlated with incident depression. Female sex was strongly associated with higher depression incidence in the univariate analysis (9% minor and 10% major depressive episodes vs. 7 and 4% in males, $p = 0.003$). However, after multivariate adjustment, gender lost its predictive power, since women were in higher NYHA classes, had lower physical functioning and more often a self-reported history of depression at baseline (Fig. 1). With inclusion of these co-variables into the regression model, gender was no longer a significant predictor ($p = 0.33$). Similarly, several other predictors lost significance in the final regression model.

Table 2 lists baseline variables which emerged as independent predictors of incident minor or major depression. Besides a self-reported history of depression only cardiac resuscitation, current smoking, frequent visits to general practitioners, NYHA class, PHQ-9 sum-score and SF-36 physical functioning proved independently predictive. Fig. 2 illustrates that the incidence of depression was closely associated with the number of independent risk factors. With more than three risk factors present incidence rates of minor and major depression were 16% and 23%, respectively.

To take possible selection bias into consideration, we compared incident minor and major depression rates as predicted in the study