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Review

Depression after heart failure and risk of cardiovascular and all-cause mortality: A meta-analysis

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ABSTRACT

Objectives. The aim of this study is to investigate whether depression after heart failure (HF) was a predictor for subsequent cardiovascular and all-cause mortality in prospective observational studies.

Methods. Pubmed, Embase, and PsycInfo databases were searched for prospective studies reported depression after HF and subsequent risk of cardiovascular or all-cause mortality (prior to May 2013). Pooled adjust hazard ratio (HR) and corresponding 95% confidence intervals (CI) were calculated separately for categorical risk estimates.

Results. Nine studies with 4012 HF patients were identified and analyzed. Pooled HR of all-cause mortality was 1.51 (95% CI 1.19–1.91) for depression compared with non-depressive patients. Subgroup analyses showed that major depression significantly increased all-cause mortality (HR = 1.98, 95% CI 1.23–3.19), but not mild depression (HR = 1.04, 95% CI 0.75–1.45). Pooled HR of cardiovascular mortality was 2.19 (95% CI 1.46–3.29) for depression compared with non-depressive patients.

Conclusion. Major depression after HF was a predictor for subsequent all-cause mortality, but not mild depression. More well-designed studies are needed to explore the influence of depression and antidepressant medication use on cardiovascular and all-cause mortality in HF patients.

Contents

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Introduction

Heart failure (HF) is a clinical syndrome that is increasing in prevalence and incidence worldwide. Despite substantial advances in its treatment, morbidity and mortality remain high (Dickstein et al., 2008; Veien et al., 2011). Therefore, early detection of high-risk patients would facilitate preventing HF and would further lower HF mortality (Nair et al., 2012). Depressive symptoms are common among patients with HF, and the prevalence of depressive symptoms in patients with HF ranges from 9% to 60% (Rutledge et al., 2006). Both major depression and the presence of depressive symptoms have been reported to increase the risks of mortality and other adverse outcomes in patients with coexistence of HF (Faris et al., 2002; Jiang et al., 2004; Junger et al., 2005; Murberg and Furze, 2004; Rumsfeld et al., 2005).

Based on the previously published clinical evidence, a well designed meta-analysis (Rutledge et al., 2006) showed that depressive symptoms or a depressive disorder increased 2-fold risk of combined endpoints (death and secondary events) in patients with HF, and the prevalence of depression among patients with HF was 21.5%. However, there were high heterogeneity with respect to the composition of the samples, study design and methods used to assess depression. After that, more prospective studies (Adams et al., 2012; Faller et al., 2007; Kato et al., 2009; Lesman-Leegte et al., 2009; Moraska et al., 2013; O'Connor et al., 2008; Rollman et al., 2012; van den Broek et al., 2011; Zuluaga et al., 2010) have been published addressing the association between depression status after heart failure and subsequent risk of mortality. To the best of our knowledge, no meta-analysis of such studies has been conducted on the association between depression after HF and subsequent risk of cardiovascular and all-cause mortality. Conflicting results whether depressive symptoms are an independent risk factor for cardiovascular and all-cause mortality remained (Faller et al., 2007; Moraska et al., 2013; Zuluaga et al., 2010).

Given above reasons, a meta-analysis may help clarify this issue. The aim of the current meta-analysis was to evaluate findings from the available prospective studies on depression after HF and subsequent risk of mortality, and determine whether depression after HF was a predictor of subsequent cardiovascular and all-cause mortality.

Patients and methods

Literature search

We conducted a literature research through Pubmed, Embase, and PsycInfo databases (prior to May 2013) for studies reporting the association between depression status after heart failure and subsequent risk of cardiovascular and all-cause mortality. Only papers published in English language were considered. Potentially relevant studies included the word 'depression', 'depressive' plus at least one of the following terms: mortality/heart failure and death/heart failure; prospective and follow-up. In addition, we also manually searched the reference lists of all identified relevant publications to detect additional eligible studies.

Study selection

Criteria for papers to be included in the current meta-analysis consisted of 1) describing prospective relationships between depression status after HF diagnosis and cardiovascular and all-cause mortality; 2) providing adjusted hazard ratio (HR) and the 95% confidence interval (CI) dealing with the risk of cardiovascular and all-cause mortality with depressive patients compared with non-depressive individuals; and 3) follow-up duration of at least 1 year. For multiple publications in the same research group, only the most recent publication was included. The definition of major and mild depression was defined by individual studies by the different depression scales (Table 1). Studies were excluded if 1) a case–control study or retrospective study; 2) unadjusted HR was reported; and 3) describing results as continuous or quantitative scores without any dichotomization around a standardized cut-off value for depression.

Data extraction and quality assessment

Two reviewers (WD Yu and HJ Fan) independently extracted the data from each study. The most fully adjusted HR and 95% CI were extracted. We also extracted the following items from individual study: author; year of publication; region; depression definitions and measures; antidepressants treatment; time of follow-up; the sample size, gender, and age of patients; death events; follow-up duration, and statistical adjustments for confounding factors. Quality assessment was performed with the following checklists based on the Meta-analysis of Observational Studies in Epidemiology guidelines (Stroup et al., 2000).

Statistical analyses

Data analyses used the most fully adjusted HR and 95% CI. For papers providing both major and minor depression data, we pooled the separate data based on the major depression and minor depression category. Homogeneity of HR across studies was assessed using the Cochrane Q statistic ($p < 0.10$ was indicated significant heterogeneity) and I^2 statistic (values of more than 50% was considered significant heterogeneity) (Higgins et al., 2003). As there was substantial heterogeneity in the types of depression and diagnosis between the different studies, a random effects model was used to calculate the pooled HR. The possibility of publication bias was assessed by Begg's rank correlation test (Begg and Mazumdar, 1994) and Egger linear regression test at $p < 0.10$ (Egger et al., 1997). Finally, sensitivity analyses were carried out by sequentially omitting one study at each turn. All analyses were conducted using STATA version 12.0 (Stata Corp LP, College Station). $P < 0.05$ was considered as statistically significant.

Results

Literature search

Following the application of the predefined search strategy, a total of 593 relevant papers were identified in our literature search. After screening the abstracts or titles, 541 studies were excluded because they were reviews, retrospective studies, or not relevant to our review. After reading the full texts, nine studies (Adams et al., 2012; Faller et al., 2007; Junger et al., 2005; Kato et al., 2009; Lesman-Leegte et al., 2009; Moraska et al., 2013; Rollman et al., 2012; van den Broek et al., 2011; Zuluaga et al., 2010) were satisfied the inclusion/exclusion. Fig. 1 presented a flow chart of the study selection.

Study characteristics and quality assessment

Nine studies with 4012 HF patients (1652 with and 2360 without depressive subjects) were identified and analyzed. The year of publication ranged from 2005 to 2013. All articles were in English. The follow-up duration ranged between 12 months and 11 years. Among these 9 articles, the assessment of depression varied across studies, with Patient Health Questionnaire (PHQ) (Faller et al., 2007; Moraska et al., 2013; Rollman et al., 2012), Center for Epidemiologic Studies Depression Scale (CES-D) (Kato et al., 2009; Lesman-Leegte et al., 2009; van den Broek et al., 2011), Beck Depression Inventory (BDI) (Adams et al., 2012; O'Connor et al., 2008), Geriatric Depression Scale (GDS) (Zuluaga et al., 2010),and Hospital Anxiety and Depression Scale (HADS) (Junger et al., 2005). The characteristics of the included studies were listed in Table 1. Supplement Table S1 presented the qualities of the included studies. All the included studies stated clear inclusion and exclusion criteria, clear definition of outcome, adjusted important confounders, and performed the appropriate statistics. However, most of studies were followed less than 5 years.

All-cause mortality

Seven studies (Adams et al., 2012; Junger et al., 2005; Kato et al., 2009; Moraska et al., 2013; Rollman et al., 2012; van den Broek et al., 2011; Zuluaga et al., 2010) reported on all-cause mortality for depression. The total number of participants included in this meta-analysis