



Original article

Impact of clustered depression and anxiety on mortality and rehospitalization in patients with heart failure[☆]



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ABSTRACT

Background: Anxiety is often present in patients with depression. The aim of this study was to evaluate the impact of clustered depression and anxiety on mortality and rehospitalization in hospitalized patients with heart failure (HF).

Methods: A total of 221 hospitalized patients with HF, who completed the questionnaires, were analyzed in this prospective study (mean age 62 ± 13 years; 28% female). One-third patients had implanted cardiac devices. Depression was defined as a Zung Self-Rating Depression Scale index score of ≥ 60 and anxiety was defined as a State-Trait Anxiety Inventory score of ≥ 40 (male) or ≥ 42 (female). The primary outcome was the composite of death from any cause or rehospitalization due to worsened HF and refractory arrhythmia.

Results: Of the 221 HF patients, 29 (13%) had depression alone, 80 (36%) had anxiety alone, and 46 patients (21%) had both depression and anxiety. During an average follow-up of 41 ± 21 months, patients with depression alone and those with clustered depression and anxiety were at an increased risk of the primary outcome [hazard ratio (HR) 2.24, 95% confidence interval (CI): 1.17–4.28, $p = 0.01$ and HR 2.75, 95% CI: 1.51–4.99, $p = 0.01$, respectively] compared to patients with no symptoms. Multivariate analysis after adjusting for age, gender, New York Heart Association functional class, B-type natriuretic peptide, device implantation, renal dysfunction, and left ventricular dysfunction showed clustered depression and anxiety, but not depression alone or anxiety alone, was an independent predictor of the primary outcome (HR 1.96, 95% CI: 1.00–3.27, $p = 0.04$).

Conclusions: Our results showed that clustered depression and anxiety were associated with worse outcomes in patients with HF.

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Introduction

Heart failure (HF) is caused from most types of heart diseases and is a chronic and progressive condition that is a major cause of

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morbidity and mortality [1]. The psychological issues, particularly emotional distress including depression and anxiety, are common in patients with HF [1–5]. Several studies have focused on the role of depression and suggested that depression is a possible risk factor for adverse outcomes in patients with HF [4–7]. The prevalence of depression is reported to be approximately 15–40% in patients with HF, and depression is independently associated with poor outcomes [5–13]. A meta-analysis showed that depression is common among patients with HF, and substantially higher rates of clinically significant depression are present among patients with more severe HF [4].

There have been fewer studies regarding anxiety in patients with HF. A previous report showed that 18.4% of patients with

HF had an anxiety disorder [14]. Another report showed that the score for anxiety symptoms was higher in patients with HF than in healthy controls [15]. However, this issue has remained controversial [1]. In some studies, no association has been found between anxiety symptoms and cardiac events in patients with HF [16–19].

Recently, van den Broek et al. [20] focused on the impact of clustering psychosocial risk factors on clinical outcomes in patients with implantable cardioverter defibrillators (ICDs) and showed that ICD patients with both anxiety and Type D personality were at an increased risk of ventricular arrhythmia. In that study, the risk factors were clustered because psychological risk factors often occurred together, but not individually, and the clustering of psychological risk factors may pose a high-risk factor for clinical events than would a single risk factor in cardiac patients [20,21]. Although depression and anxiety have been discussed separately as psychological factors, they frequently cluster within a patient [22]. The signs and symptoms of anxiety are often present in patients with depression, and the two conditions may play a partial role in a pathophysiological process of HF [23]. Some studies have shown that the clustered depression and anxiety worsened patients' health status following myocardial infarction or percutaneous coronary intervention [24,25]. From this viewpoint, clustered depression and anxiety may be clinically valuable as an indicator of psychological distress in patients with HF. However, a few studies have investigated this issue. The aim of this study was to evaluate the effect of clustered depression and anxiety on mortality and rehospitalization in patients with HF.

Methods

We conducted a substudy of the prospective observational study comprising hospitalized patients with cardiovascular disease, who were admitted to the Cardiology Department of Tokyo Women's Medical University Hospital between June 2006 and April 2008. Patients with dementia, delirium, or other conditions (e.g. unconsciousness, intensive care, and end stage of another life-threatening disease) that make completing self-reported written questionnaires difficult were excluded. Among them, 221 patients with a New York Heart Association (NYHA) functional class ≥ 2 on admission, who were diagnosed with HF, and who completed the questionnaires were included in this study (Fig. 1). The details of

the study have been reported elsewhere [26]. The protocol was approved by the institutional review board of Tokyo Women's Medical University. All patients gave written informed consent.

Assessment of depression and anxiety

The majority of patients received the psychological questionnaires within 3 days (2 ± 1 days) after their admission to the hospital. For patients who initially required intensive treatment, these questionnaires were received after their transfer to the general cardiology ward. The Zung Self-Rating Depression Scale (SDS) was used to screen for depression and to measure the severity of the depression in a number of settings [27–31]. The Zung SDS is a self-reported scale containing 20 questions that assess the psychological and somatic symptoms. The Zung SDS score has been reported to be a primary discriminating variable in distinguishing depressed from non-depressed persons and indicates likelihood ratio positive for major depression as 3.3 [95% confidence interval (CI): 1.3–8.1] and likelihood ratio negative as 0.35 (95% CI: 0.2–0.8) [29]. The Zung SDS score has also been used to assess depression in clinical studies on cardiovascular diseases [32–36]. A cutoff index score of 60 has been shown to detect clinical depression while avoiding an abundance of false positives in sick patients [37–40]. In this study, depression was defined as a Zung SDS index score of ≥ 60 .

The State-Trait Anxiety Inventory (STAI) was used to measure anxiety symptoms [41]. In this study, only the state-scale measurement was used because state anxiety is characterized as a temporary change in each patient's emotional state due to medical illness or other external cause, the measurement has also been used in clinical studies on cardiovascular diseases [16,20,42]. The STAI comprises 20 items, and each item is scored on a four-point scale from 1 (not at all) to 4 (very much so). The STAI scores range from 20 to 80, with higher scores indicating greater levels of anxiety. Anxiety was defined as a score of ≥ 40 (male) or ≥ 42 (female) [43,44].

Follow-up

After discharge, patients were seen as outpatients at our hospital or their general practitioner's clinic at 1- to 3-month intervals until October 2011. Patients receiving pacing device therapy, including pacemakers, cardiac resynchronization therapy (CRT), and ICD, were also followed every 3–6 months at our pacemaker/ICD clinic. The information about deceased patients was obtained from the medical records, family members, their general practitioners, and the admitting hospital.

Clinical outcomes

The primary outcome was the composite of death from any cause and rehospitalization due to worsened HF and refractory arrhythmia from the time of enrollment to the first event. Worsened HF was defined by signs and symptoms, such as dyspnea, rales, and ankle edema, as well as by the need for treatment with diuretics, vasodilators, positive inotropic drugs, or an intra-aortic balloon pump. Refractory arrhythmia was defined as supraventricular or ventricular tachyarrhythmia that required external defibrillation or pacing, intravenous antiarrhythmics, such as amiodarone and nifekalant, catheter ablation, or implantation of an ICD, or bradyarrhythmia that required implantation of a pacemaker. Both supraventricular and ventricular arrhythmias are common in patients with HF, and cause symptoms, hemodynamic instability, and morbidities such as stroke and sudden death. Therefore, we included rehospitalization for refractory arrhythmia in

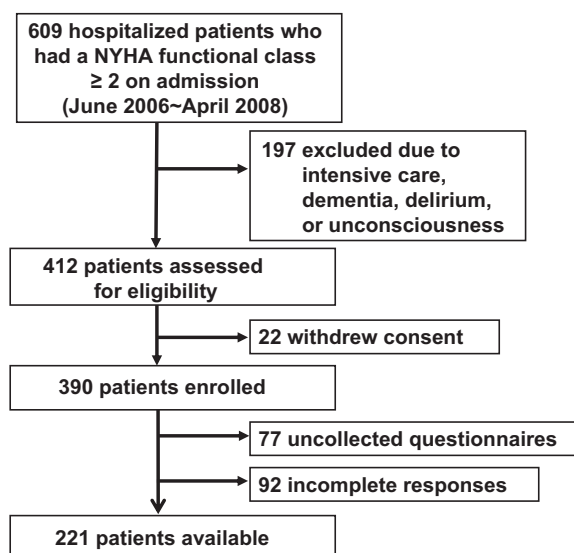


Fig. 1. The flow diagram of study subjects. NYHA, New York Heart Association.

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