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Association of anxious and depressive symptoms with medication nonadherence in patients with stable coronary artery disease

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ABSTRACT

Objective: Depression and anxiety lead to increased morbidity and mortality in patients with coronary artery disease (CAD). Medication nonadherence is one possible pathway contributing to adverse outcome, but it is unknown how either depression or anxiety itself influences adherence compared to combined depressive–anxious comorbidity. The aim of the study was to evaluate the influence of simultaneous depressive and anxious symptoms on medication adherence in patients with stable CAD.
Methods: Between 02/2009 and 06/2010 we examined the association between current depressive and anxious symptoms with medication nonadherence in a cross-sectional study of 606 inpatients with stable CAD. Symptoms were assessed by using the Hospital Anxiety and Depression Scale. Morisky Medical Adherence Scale measured medication adherence.
Results: Depressive and anxious symptoms were weakly and independently associated with medication nonadherence ($r=0.28$, $p<0.01$ and $r=0.27$, $p<0.01$ respectively). Compared to non-depressed, patients with depressive symptoms had an up to 3.6-fold odds, those with anxious symptoms an up to 3.2-fold odds of nonadherence. The presence of combined anxiety and depressive symptoms was also weakly correlated with adherence ($r=0.30$, $p<0.01$). The risk for nonadherence in patients suffering from both anxiety and depression was up to 4.4 times higher compared to patients without symptoms.
Conclusion: Apart from depressive symptoms, anxiety is a second important and independent marker for nonadherence in patients with coronary artery disease. The negative effect of anxiety on medication adherence increases in case of comorbid depressive symptoms. Future studies addressing medication adherence should focus more on anxious-depressive comorbidity than on singular depressive or anxious symptoms.

Introduction

Mental disorders, especially anxiety and depression, are common in patients with coronary artery disease [1–3]. Both are associated with a higher risk for increased morbidity and mortality: While the effect of depression on prognosis is established and well-known [4–8], the knowledge of the influence of anxiety is quiet new. A recent meta-analysis showed that anxious patients have a 26% increased risk of suffering from a coronary artery disease and a 48% increased risk of cardiac death [9].

One of the suggested pathways linking mental disorders and decreased prognosis in patients with coronary artery disease is medication nonadherence [1,10]. A meta-analysis showed that in a population of patients with chronic diseases the odds of medication nonadherence are up to 3-times greater in depressed than in non-depressed patients [10,11]. The average effect of anxiety in the meta-analysis, however, was close to zero as a result of values deviating between −0.64 and 0.39 [10]. Until now, the relationship between anxiety and medication nonadherence remains unclear.

Recently, Bauer et al. reported an independent impact of depressive and anxious symptoms, respectively, on adherence in a sample of patients with cardiac diseases in general. However, they could not make any statements regarding the impact of depressive–anxious co-morbidity on adherence in these patients due to a limited number of participants ($n=134$) [12].

The present study examines the association between anxiety, depression, and medication adherence in a large sample of patients with stable coronary artery disease (CAD). The study also focuses on the association of comorbid anxious and depressive symptoms, and medication adherence, a constellation which to our knowledge has not been investigated up to now, neither in patients with CAD nor in those with chronic diseases in general.

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We hypothesize that in our sample depressive and anxious symptoms are independently associated with medication nonadherence. The strongest association is expected in patients with comorbid anxious and depressive symptoms.

Methods

Study design and participants

The study was performed as a cross-sectional study in agreement with the Ethics Committee of the faculty of clinical medicine of the University of Heidelberg, based on the Declaration of Helsinki of 1964 (Ethics Committee vote S-293/2008). Between February 2009 and June 2010 patients were screened on three internal medicine inpatients wards of the University Hospital Heidelberg. Patients were considered for inclusion if they were between 18 and 75 years old, German-speaking, if they had a CAD confirmed by a recent coronary angiogram (within 3 months) and gave written informed consent. Criteria for CAD were defined as having an actual stenosis of at least 50% in one or more major coronary arteries or having a history of myocardial infarction, coronary artery bypass surgery or angioplasty. Patients with severe heart failure (NYHA IV), acute life-threatening conditions (as progressive cancer disease or history of organ transplantation), severe chronic inflammatory disease (as borreliosis, HIV-infection or chronic hepatitis), inflammatory bowel diseases and severe obstructive lung diseases were excluded. Patients with current severe depressive disorder, psychosis, delirium or dementia were also not been considered.

The data of our study were collected parallel to those of the SPIRR-CAD-Study [13], a randomised, controlled, multi-centre clinical trial which evaluates the effect of a stepwise psychotherapy intervention for reducing risk in patients with CAD. It has to be mentioned that the patients were first informed about the course of SPIRR-CAD after having been screened for mental disorders. So, participants of our study completed the handed questionnaires without being influenced by another trial.

Measurement of depressive and anxious symptoms

Depressive and anxious symptoms were assessed by using the Hospital Anxiety and Depression Scale (HADS), a self-rating instrument developed by Zigmond and Snaith in 1983 to measure severity of anxiety and depressive symptoms in physically ill patients [14]. In a large sample of studies the HADS has shown good internal consistency [15] and satisfiable test–retest reliability over short intervals as well as good sensitivity to changes of affective symptoms [16]. The German Version used in this study has initially been validated in cardiological patients and has been recommended as a routine screening tool for affective disorders in this group by the test authors [17]. The questionnaire contains 14 items split into 2 different subscales (depression and anxiety). Compared to other established rating-scales for depression and anxiety both subscales have shown high correlations [15]. The scores of each subscale range from 0 points (no symptoms) to 21 points (maximum of symptoms). With regard to the recommended classification of the test authors we categorized participants as having no symptoms (HADS score of 0–7), mild symptoms (HADS score 8–10) and severe symptoms (HADS score 11–21) [17].

Measurement of medication adherence

Medication adherence was measured by using the Morisky Medical Adherence Scale (MMAS). The self-rating scale was developed and validated by Morisky et al. in 1986 to predict whether patients adhere to their medications or not [18]. It has been used in a wide sample of chronic diseases, especially in cardiovascular patients [18–21]. The questionnaire contains in total 4 items. The summary score range from 0 points (optimum of adherence) to 4 points (maximum of nonadherence). Following the classification of former studies having used the MMAS in patients with CAD we categorized 0–1 point as having good medication adherence, 2–4 points as having poor medication adherence [21].

Other parameters assessed

Besides measuring psychic symptoms and medication adherence we registered age and gender of all patients.

Statistical analysis

Assessed data were fed into 2 copies of the same access data base by two different persons. After electronic comparison the data were corrected manually in case of deviation.

The analysis did not consider MMAS scores, if one single item was missing. In case of the HADS we tolerated up to 2 missing values of each subscale replacing it with the mean of the remaining 5 items. Subscales with more than 2 missing values were excluded. Differences in characteristics between participants were compared using a 2-sample *t*-test. We correlated the scores of the anxiety subscale and the depression subscale as independent variable with the MMAS score as dependent variable linearly in order to describe the association between depressive symptoms, anxious symptoms and medication adherence. Multiple regression models were used to prove independence of the found correlations. Afterwards, we divided anxious and depressive symptoms in categories of different severity and medication adherence in groups of adherent and nonadherent participants. To exemplify the associations found between psychic symptoms and medication nonadherence we calculated the corresponding relative risks using the categorized data.

Finally age and gender were correlated with the summary score of MMAS to describe the influence of socio-demographic data. All analyses were performed using statistical analysis software (SAS Version 9.2).

Results

Descriptive data

In total, 606 persons participated in the study. Their mean age was 62.5 ± 9.1 years, with a range of 25–75 years. 76.6% of participants were male. Women were significant older than men (64.60 ± 8.69 years vs. 61.88 ± 9.11 years, $p<0.01$). Due to exclusion criteria more than 40% (760/1765) of the screened patients were ruled out. 399 persons did not give informed consent and were excluded, too (Fig. 1). Compared to patients included the part of male patients excluded was higher (76.6% and 75.8%, respectively, $p=0.73$). However, mean age does not differ significantly between both groups (62.5 ± 9.1 years and 64.3 ± 8.5 years, respectively, $p<0.01$).

Table 1 provides an overview of mean HADS and MMAS score separated by age and gender of participants. In total, 137 of 606 participants (22.6%) did not take their medications as prescribed. Overall, 253 of 606 participants (41.7%) reported having at least mild or severe symptoms of the screened mental disorders. A total of 24.4% (148/606) showed current depressive symptoms and 35.5% (215/606) showed current anxious symptoms. 18.2% (110 of 606) suffered from depressive and anxious symptoms simultaneously. Depressive symptoms were 3 times more frequently in combination with anxious symptoms than alone (74.3% versus 25.6%).

Depressive symptoms and medication adherence

Medication nonadherence increases with the severity of depressive symptoms (Table 2). A total of 15.3% (70/458) of patients with no symptoms (HADS-D<8) reported not to take their medication compared with 39.6% (36/91) of patients with mild (8≤HADS D≤10) and 54.5% (31/57) with severe depressive symptoms (HADS-D≥11) (Fig. 2). Compared to patients who reported having no symptoms, those with severe symptoms had a 3.6 times higher risk of being nonadherent to prescribed medication.

Statistical analysis showed a weak negative correlation of depressive symptoms and medication adherence ($r=-0.28$, $p<0.01$).