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Original article

# Frequency and clinical correlates of bipolar features in acute coronary syndrome patients

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ABSTRACT

*Background:* Depression and acute coronary syndrome (ACS) are both extremely prevalent diseases. Studies aimed at evaluating whether depression is an independent risk factor for cardiac events provided no definitive results. In most of these studies, depression has been broadly defined with no differentiation between unipolar (MDD) versus bipolar forms (BD). The aim of this study was to evaluate the frequency of DSM-IV BD (bipolar I and bipolar II subtypes, cyclothymia), as well as temperamental or isolated bipolar features in a sample of 171 patients hospitalized for ACS. We also explored whether these psychopathological conditions were associated with some clinical characteristics of ACS.
*Methods:* Patients with ACS admitted to three neighboring Cardiac Intensive Care Units (CICUs) in a 12-month continuative period of time were eligible for inclusion if they met the criteria for either acute myocardial infarct with or without ST-segment elevation or unstable angina, verified by standard ACS criteria. All patients underwent standardized cardiological and psychopathological evaluations.
*Results:* Of the 171 ACS patients enrolled, 37 patients (21.7%) were found to have a DSM-IV mood disorder. Of these, 20 (11.7%) had bipolar type I or type II or cyclothymia, while 17 (10%) were the cases of MDD. Rapid mood switches ranged from 11% of ACS patients with no mood disorders, to 47% of those with MDD to 55% of those with BD. Linear regression analysis showed that a diagnosis of BD ($p = .023$), but not that of MDD ($p = .721$), was associated with a significant younger age at the index episode of ACS. A history of previous coronary events was more frequent in ACS patients with BD than in those with MDD.
*Conclusions:* Our data indicate that bipolar features and diagnosis are frequent in ACS patients. Bipolar disorder has a negative impact on cardiac symptomatology. Further research in this area is warranted.


## 1. Introduction

It is well known that depression is highly prevalent among patients with acute coronary syndrome (ACS). The syndrome of major depression is present in approximately 15–23% of patients with cardiac disease, including those suffering from ACS [21,29]. Such rates are substantially higher than that seen in the general population (4 to 5%) or primary care patients (8 to 10%) making depression a condition affecting millions of patients with ACS annually [26,40]. Depression is a risk factor for the development of ACS, and worsens outcome when present in patients with established ACS, suggesting that depression is associated with both physiological and psychosocial changes that are deleterious to the cardiovascular system [12,19,34,37]. Depressive disorders increase the risk of rehospitalization after myocardial infarction and their treatment were found to have a positive impact on cardiac outcome [5,7,21,33].

Compared to the large body of literature on major depression and ACS, the association between bipolar disorder and ACS received less attention by researchers. Data from the National Comorbidity Survey Replication (NCS-R) showed that cardiovascular diseases are associated with bipolar disorder in women (OR = 2.8) after controlling for obesity, high blood pressure, smoking, diabetes and anxiety disorders [15]. Other studies

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reported that subjects with bipolar disorder show a two-fold cardiovascular mortality when compared with general population estimates [2,16,31]. Rush et al. [35] examined the association between mood symptoms and 10-year CVD risk estimated by Framingham risk score in a cohort of patients with bipolar disorder. They found that depressive symptoms were strongly associated with increased odds of long-term CVD risk. Depressive symptoms were also significantly associated with elevated blood pressure, glucose and BMI in bipolar patients.

The reasons for such associations have yet to be determined. Several studies in patients with BD observed an activation of pro-inflammatory cytokines during manic, depressed or euthymic episodes of bipolar illness; some markers seem to be more specifically related to bipolar disorder than to major depression [3]. Metabolic syndrome, a composite measure of many cardiovascular risk factors, is more common in patients with bipolar disorder than in the general population and may at least in part account for the increased cardiovascular risk in this population [39]. Intriguingly, manic/hypomanic symptom burden has been shown to predict cardiovascular mortality [16] and endothelial dysfunction [17], raising questions about other explanations for elevated cardiovascular risk among bipolar patients. For example, in the Zurich Cohort Study, Angst et al. [2] found that group with bipolar I or II disorder had the highest risk for cardiovascular deaths and the group with major depression the highest for deaths by suicide.

All these data derive from studies conducted in samples of patients with bipolar disorder. However, we are unaware of any studies evaluating the frequency and clinical correlates of bipolar disorder in a clinical sample of patients with coronary heart disease. The aim of our study was to explore frequency of bipolar disorders (type I and type II and cyclothymia) and bipolar features (affective temperaments, euphoric and mixed states indicators) in a sample of 171 patients with ACS afferent to three neighboring acute cardiac units in a defined period of time. In particular, we were interested in evaluating whether bipolarity was associated to different clinical characteristics of ACS. The study was conducted within the framework of a prospective follow-up study of ACS patients.

## 2. Methods

### 2.1. Study population

Patients with ACS admitted to three Cardiac Intensive Care Units (CICUs) were eligible for inclusion if they met the criteria for either acute myocardial infarct with ST-segment elevation (STEMI) or without ST-segment elevation (NSTEMI) or unstable angina (UA), verified by standard ACS criteria. The three units were located in a northwest area of Italy, with an average distance of 40 miles from each other and serving similar geographic catchment areas in terms of socio-demographic characteristics. Exclusion criteria were neoplastic disease, severe pulmonary, hepatic or renal insufficiency, infections requiring antibiotics, autoimmune disease, immunosuppressive therapy, severe anaemia and severe degenerative disease of the central nervous system.

Two comparisons groups, one with mood disorders without cardiovascular risk factors and one of healthy individual with no mental or physical illness, were recruited to investigate biological and genetic correlates (data not presented here). The study was conducted in accordance with the Declaration of Helsinki, was approved by the local ethics committees and written informed consent was obtained from all patients.

### 2.2. Cardiological evaluation

Data on patients' demographics, medical history, clinical characteristics, electrocardiographic findings, ACS definition and treatment interventions, as well as in-hospital outcomes were reported in a detailed standardized case record form, adapted from the Blitz Study [8], by a trained cardiologist in each CICU. The details on symptoms onset, first medical help seeking and arrival at hospital CICU were collected as soon as patients could be interviewed. Particular care was taken in assessing the timing of hospital CICU arrival, ECG execution, and reperfusion treatment. Additional items included length of stay in the CICU and overall hospital stay, timing of invasive procedures and transfer to a tertiary care hospital to undergo coronary angiography and/or revascularization.

### 2.3. Risk factors evaluation

All subjects were assessed at the time of enrolment for the following measures: resting blood pressure, cardiovascular risk factors, including tobacco smoking, diabetes mellitus, hypercholesterolemia and hypertension. The body height and weight, blood pressure, and body mass index (BMI) of all subjects were measured. Hypertension was defined as either resting systolic or diastolic blood pressure greater or equal to 140/90 mmHg at two different times or on antihypertensive medications. Diabetes mellitus was defined as a serum fasting glucose greater or equal to 7.1 mmol/l or on hypoglycemic medications. Hypercholesterolemia was defined as a fasting total serum cholesterol level greater or equal to 4.9 mmol/l or on anti-cholesterol drugs. Smoking status was recorded as current smoker or past smoker.

Fasting blood samples were obtained from all subjects to determine serum creatinine, glucose, C-reactive protein level and lipid levels.

### 2.4. Psychiatric assessment

All patients were evaluated by the Structured Clinical Interview for Psychiatric Disorders (SCID-I) [18] to determine the presence of Axis I psychiatric disorders according to DSM-IV criteria. Data on use of psychotropic medications was collected in the SCID-I appropriate section.

#### 2.4.1. 17-Item Hamilton depression rating scale (HDRS)

The presence and severity of current depression was assessed by the 17-Item HDRS [22]. The HDRS provides an indication of depression and, over time, a guide to recovery. It is widely used and accepted outcome measures for evaluating the severity of depression symptoms in ACS patients. The HDRS was administered by a trained professional using a semistructured interview. Eight items are scored on a 5-point scale, ranging from 0 = not present to 4 = severe. Nine are scored from 0–2. Scores below or of 5 define the absence of clinically relevant depression; scores between 6 and 13 indicate mild depression; from 14 to 18 moderate depression; from 19 to above severe depression [35].

#### 2.4.2. Beck depression inventory-II (BDI-II)

Baseline depressive symptms were also evaluated by the BDI-II [4]. The BDI-II contains 21 questions, each answer being scored on a scale value of 0 to 3. The cutoffs used differ from the original: 0–13: minimal depression; 14–19: mild depression; 20–28: moderate depression; and 29–63: severe depression. Higher total scores indicate more severe depressive symptoms. The BDI-II showed concurrent validity with the Hamilton Depression Rating Scale. The BDI-II evaluates two components: the affective component (e.g., mood) and the physical or "somatic" component (e.g., loss of appetite). The purpose of the two subscales is to help determine the primary component of a patient's depression.