ORIGINAL ARTICLE

Observational Study

Childhood trauma and factors associated with depression among inpatients with cardiovascular disease

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Abstract

AIM

To identify factors associated with depressive symptoms

among inpatients with cardiovascular disease (CVD).

METHODS
This is a cross-sectional study performed in a subsample of a large cross-sectional research that investigated affective disorders and suicide behaviour among inpatients hospitalized in non-surgical wards of the University Hospital of the Federal University of Minas Gerais from November 2013 to October 2015. Sociodemographic and clinical data were obtained through a structured interview and medical record review. Depression was assessed by the depression subscale of the Hospital Anxiety and Depression Scale, with scores ⩾ 8 considered as positive screening for depression. We used the Fagerström Test for Nicotine Dependence to characterize nicotine dependence. For assessing resilience and early-life trauma, we used the raw scores of the Wagnild and Young Resilience Scale and Childhood Trauma Questionnaire, respectively.

RESULTS
At endpoint, we included 137 subjects. Thirty-eight (27.7%) subjects presented depressive symptoms and nine (23.7%) of those were receiving antidepressant treatment during hospitalization. The female sex; a lower mean educational level; a greater prevalence of previous suicide attempts; a higher level of pain; a higher prevalence of family antecedents of mental disorders; a lower resilience score; and higher childhood trauma score were the factors significantly associated with screening positive for major depression ($P < 0.05$). Multivariate analysis demonstrated that the factors independently associated with the depressive symptoms were a higher childhood trauma severity (OR = 1.06; $P = 0.004$); moderate to severe nicotine dependence (OR = 8.58; $P = 0.008$); and the number of previous hospital admissions (OR = 1.11; $P = 0.034$). The obtained logistic model was considered valid, indicating that the three factors together distinguished between having or not depressive symptoms, and correctly classified 74.6% of individuals in the sample.

CONCLUSION
Our results demonstrate that inpatients presenting both CVD and a positive screening for depression are more prone to have antecedents of childhood trauma, nicotine dependence and a higher number of previous hospitalizations.

Key words: Inpatients; Depression; Cardiovascular disease; Depressive symptoms; General hospital

Core tip: The prevalence of depression is considerably higher among individuals with cardiovascular diseases (CVD) when compared to the general population. Both major depression and depressive symptoms are predictors of poor outcome in patients with CVD. Depressive disorder is frequently overlooked and untreated in individuals with CVD. Our results demonstrate that

inpatients presenting both CVD and a positive screening for depression are more prone to have antecedents of childhood trauma, nicotine dependence and a higher number of previous hospitalizations. Clinicians may consider these factors in the assessment of CVD inpatients at risk for major depression. This measure can improve their treatment approach and patients' prognosis.

INTRODUCTION

The prevalence of major depressive disorder (MD) is four times higher among individuals with cardiovascular diseases (CVD) when compared to the general population[1-4], and MD is a predictor for future CVD. MD increases the risk for coronary arterial disease (CAD) by 56%, independent of other traditional cardiovascular risk factors[1]. Moreover, MD and depressive symptoms are predictors of poor outcome in patients with CVD regarding morbidity and mortality[2,3].

Maltzberg[4] first reported the bidirectional relationship between MD and CVD in 1937. This author observed an increase in mortality from CVD in patients with severe depression. More recently, some authors reported that post-myocardial infarction depression increases the risk of all-cause mortality (RR = 2.25) and of cardiac events (RR = 1.59) within 24 mo after the event[5]. Even in the absence of depressive symptoms, a positive history of depression in first-degree relatives may influence the cardiovascular risk profile in adulthood, comparing to control group[6].

Various biological modifications, previously found in patients with depression, may explain these findings. An increased concentration of inflammatory biomarkers (C-reactive protein, interleukins 1 and 6), metabolic dysregulation, dysfunctions in the platelet clotting cascade, decreased variability in heart rate, hyperactivation of hypothalamus-pituitary-adrenal axis and reduction in circulating endothelial progenitor cells are some of the factors that may be at the pathophysiological origin of the association between depression and CVD[2,7-9]. Finally, both depression and CVD have notorious genetic determinants, which may underlie the development of one and another as shared risk factors[2,10]. Even acute and chronic life stressors may increase the risk for developing one of these diseases[2,10]. Adverse events in early life can directly affect genome through epigenetic mechanisms and contribute to the expression or exacerbation of a genetic susceptibility for depression, CVD or both in adulthood[2].

During hospitalization, depression decreases inpatients'

treatment adherence, increases functional disability and extends hospital length of stay[11,12]. Inpatients with CVD presenting positive screening for depression at discharge have a 2.5 fold increase in relative risk of experiencing a CVD-related hospitalization, even after adjustment for traditional cardiovascular risk factors and measures of disease severity[13].

Depression is still a frequently overlooked and untreated condition among individuals with CVD[14,15]. The same applies for those admitted to general hospitals, a population in which 28% present criteria for depressive disorders[16]. Less than one in four cases of major depression among inpatients are correctly diagnosed by assisting physicians[14]. In addition, only half the members of the American College of Cardiologists treat depression properly, according to a national survey[17].

Inpatients with CVD have increased vulnerability for depression. Improving the knowledge on how much risk factors influence the chances of becoming depressed may improve identification of MD among this population in the general hospital setting. We hypothesized that inpatients presenting both CVD and a positive screening for major depression are more prone to be of female sex; to present personal and familiar antecedents of psychiatric disorders (*e.g.*, suicide attempts, addictions); to present worse indicators of CVD (*e.g.*, increased number of previous hospital admissions, present pain and a worse score of functionality); and present lower resilience and antecedents of childhood trauma. Our primary goal was to assess the factors mentioned above in a population of inpatients with CVD in a university hospital.

MATERIALS AND METHODS

This cross-sectional design study encompassed a sub-sample of a larger study that investigated suicide behaviour among general hospital inpatients. We included all inpatients admitted to the wards of the University Hospital of the Federal University of Minas Gerais (UH-UFMG), hospitalized from November 2013 to October 2015. The UH-UFMG is a tertiary regional reference centre.

The Committee of Ethics in Research of UFMG approved the protocol, registered with the number CAAE 13605213.3.0000.5149. We obtained written informed consent from all participants, after providing a complete description of the study. All subjects screening positive for a psychiatric disorder received consultation-liaison psychiatric evaluations.

Subjects

For the initial study, we included inpatients aged 18-year-old or older, hospitalized in a clinical ward and excluded patients hospitalized with surgical indication. In the present study, we selected all patients with a diagnosis of CVD (*e.g.*, CAD, congestive heart failure, Chagas cardiomyopathy, cardiac arrhythmia or any other cardiac disease that required hospitalization) and excluded subjects screening positive for delirium and mild to severe cognitive impairment or dementia as well as those unable to comprehend, illiterate or with major visual or hearing impairment. We summarized the inclusion procedure in the flowchart (Figure 1).

Instruments and procedures

After a clinical assessment and stabilization, we included all subjects at admission. Experienced psychiatrists, trained to perform the assessments foreseen in the study protocol, evaluated the subjects. All the scales used in this study had been previously translated and culturally adapted to Brazilian Portuguese.

We screened delirium using the Confusion Assessment Method[18] and cognitive impairment through the Montreal Cognitive Assessment[19] using 17 as a cut-off point[20].

For screening MD, we used the Hospital Anxiety and Depression Scale (HADS-d). This scale has acceptable properties for use in inpatients with CVD[21]. Scores of $\geq$ 8 indicate a positive screening for depression, according to the Brazilian validation study that issued a sensibility of 84.6% and specificity of 90.3%[22].

We used the visual analogue scale to assess pain intensity[23]. We determined the basic and instrumental activities of daily living (ADL) using the Katz Index and the Pfeffer's Functional Activities Questionnaire (PFAQ), respectively[24]. We considered scores $\geq$ 5 in the PFAQ as characteristic of dependence on instrumental ADL[25].

We considered a score $\geq$ 8 on the Alcohol Use Disorders Identification Test to assess problematic alcohol use[26] and a score $\geq$ 4 on the Fageström Test for Nicotine Dependence to characterize moderate to severe nicotine dependence[27].

We considered the levels of positive psychosocial adjustment given major life events, like resilience, and used the Wagnild and Young Resilience Scale (WYRS) to evaluate resilience level. The WYRS is a paper-and-pencil scale, composed of 25 likert-type items[28] and, as the validation study did not establish a cut-off point, we used the raw results in our analysis. For assessing early-life trauma we used the Childhood Trauma Questionnaire (CTQ)[29]. The CTQ is a 28-item self-report inventory that provides a valid screening for early life abuse or negligence.

Statistical analysis

In the descriptive analysis, we calculated measures of central tendency and dispersion. The Shapiro-Wilk test assessed data normality. For univariate analysis, a χ^2 test was considered for categorical variables and Mann-Whitney test for continuous variables. To determine which factors had a greater association with positive screening for depression in our sample, we conducted a multiple logistic regression with stepwise selection. Those variables with P value $\leq$ 0.2 in univariate analysis were apt to enter the model. The χ^2 test model and Nagelkerke's R^2 used to evaluate the predictive ability of the logistic model obtained. Calculation of odds ratios (OR) considered a 95%CI and significance of $P < 0.05$.
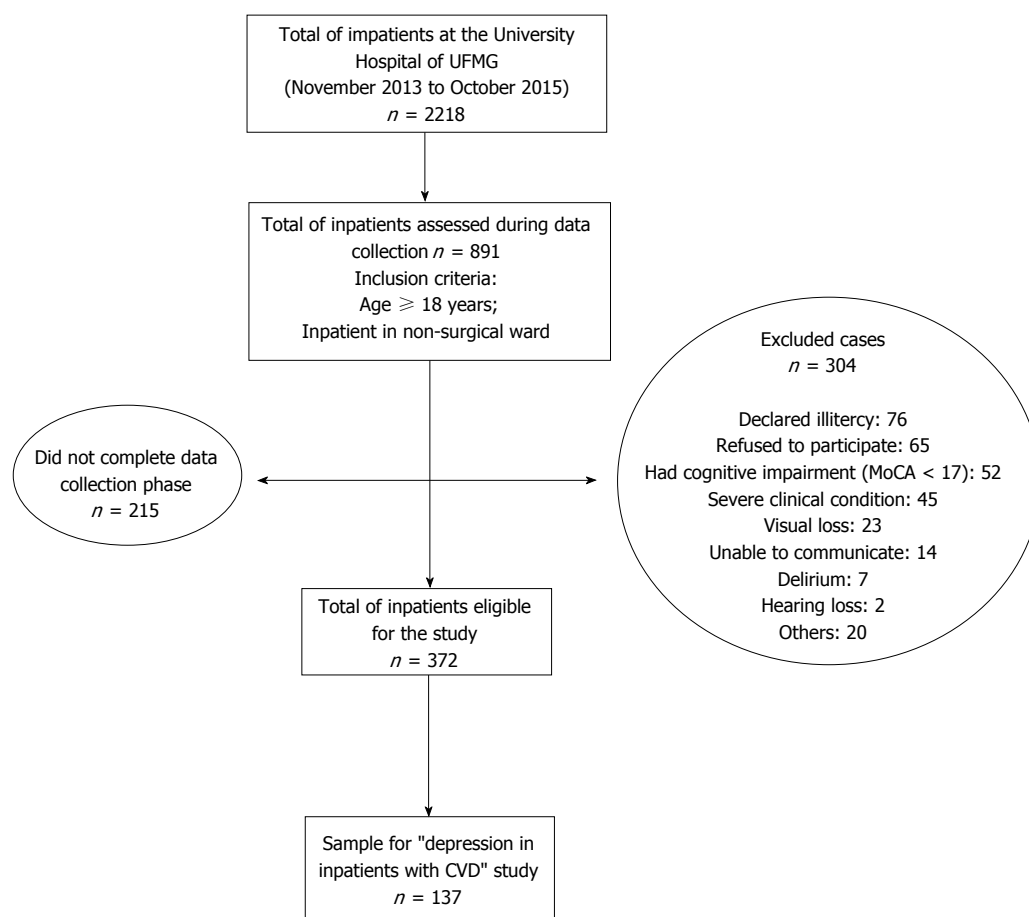
Figure 1 Flowchart of subjects included in the study. UFMG: The Federal University of Minas Gerais; CVD: Cardiovascular disease.

All analyses were performed using SPSS software version 20 (IBM Corporation© 2011).

RESULTS

Sample description

At endpoint, we included 137 subjects and found a higher prevalence of males [n = 92 (67.2%)], a mean age of 52.1 ± 12.5 years old and a mean educational level of 8.5 ± 4.4 years. The most prevalent CVD diagnoses were CAD (n = 76; 55.5%), congestive heart failure (n = 43; 31.4%) and cardiac arrhythmia (n = 15; 10.9%). CAD, the most frequent cardiovascular diagnosis, was not associated with positive screening for major depression. Seventy-five (54.7%) and 23 (16.8%) subjects presented hypertension and diabetes mellitus, respectively.

Factors associated with positive screening for depression

Thirty-eight (27.7%) subjects screened positive for depression and nine (23.7%) were taking antidepressants during hospitalization. Female sex, lower mean educational level, greater number of previous suicide attempts, higher level of pain, higher prevalence of family antecedents of mental disorders, lower resilience score and higher childhood trauma score were the factors

significantly associated to screening positive for major depression (Table 1).

Three factors remained statistically associated with a positive screening for depression (Table 2) in multivariate analysis: (1) childhood trauma; (2) moderate or severe nicotine dependence; and (3) the number of hospital admissions.

Patients with moderate and severe nicotine dependence were 8.58 times more prone to screen positive for depression (P = 0.008).

The chance to screen positive for depression increased 11% for each hospital admission (P = 0.034) and 6% for each point of increase in the CTQ score for childhood trauma (P = 0.004).

The logistic model indicated that the three factors together distinguished between positive screening for depression or not, and correctly classified 74.6% of individuals in the sample (χ^2: 17.974, P < 0.001, D.F. = 1; Nagelkerke R^2: 0.33).

DISCUSSION

This study assessed the influence of the factors associated with positive screening for depression in a sample of patients with CVD hospitalized in a university hospital. After multiple comparisons, we found that positive screening for depression was significantly associated with

Table 1 Factors associated with positive screening for depression (Hospital Anxiety and Depression scale - depression subscale score ≥ 8) in inpatients with cardiovascular diseases (*n* = 137) *n* (%)

| | Screening for depression | | Missing data (%) | *P* value |
	Yes	No		
Sociodemographic variables				
Gender				
Male	15 (39.5)	77 (77.8)	-	< 0.001[a]
Female	23 (60.5)	22 (22.2)	-	
Age, mean (SD)	53.7 ± 11.4	51.5 ± 12.8	-	0.444
Elder (aged ≥ 60 yr)	15 (39.5)	24 (24.2)	-	0.077
Educational level in years (mean ± SD)	7.4 ± 4.4	8.5 ± 4.3	1.5	0.035[b]
Married/lives with partner	25 (65.8)	70 (70.7)	0.7	0.723
Lives alone	3 (8.1)	9 (9.1)	0.7	0.857
Any son	34 (91.9)	83 (84.7)	1.5	0.272
Unemployed	9 (24.3)	23 (23.5)	1.5	0.917
Religion	35 (94.6)	91 (91.9)	0.7	0.595
Clinical variables				
N° of previous hospital admissions, mean (SD)	7.6 ± 9.1	5 ± 5.2	5.8	0.07[b]
CAD	18 (47.4)	58 (58.6)	-	0.237
Congestive heart failure	12 (31.6)	31 (31.3)	-	0.976
Cardiac arrhythymia	5 (13.3)	10 (10.1)	-	0.76
Hypertension	19 (50)	56 (56.6)	-	0.489
Diabetes mellitus	5 (13.2)	18 (18.2)	-	0.481
Pain level, mean (SD)	2.2 ± 2.9	1.3 ± 2.4	0.7	0.136
Propranolol	8 (21.1)	12 (13.5)	8.0	0.255
Dependence in basic ADL	10 (26.3)	14 (14.1)	0.7	0.09
Dependence in instrumental ADL	2 (22.2)	4 (17.4)	76.6	0.753
Psychosocial variables				
Family history of mental disorder	18 (47.4)	20 (20.2)	-	0.001[a]
Previous suicide attempt	11 (28.9)	8 (8.2)	0.7	0.002[a]
Moderate to severe nicotine dependence	7 (18.4)	10 (10.1)	-	0.186
Problematic alcohol use	7 (30.4)	13 (18.84)	32.8	0.243
Resilience score, WYS mean (SD)	138.5 ± 14.5	144.9 ± 14.9	2.9	0.029[b]
Childhood trauma score, CTQ mean (SD)	46.4 ± 20.1	37.5 ± 12.6	8.8	0.004[b]

[a]χ^2 test significant if *P* < 0.05; [b]Mann-Whitney test significant if *P* < 0.05. CAD: Coronary arterial disease; ADL: Activities of daily living; WYS: Wagnild and Young Scale; CTQ: Childhood Trauma Questionnaire.

Table 2 Logistic regression analysis of factors associated with positive screening for depression (Hospital Anxiety and Depression scale - depression subscale score ≥ 8) in inpatients with coronary arterial disease

Variable	B	EP	Wald	OR	95%CI	*P*
Moderate to severe nicotine dependence	2.15	6.91	7.135	8.58	1.77-41.57	0.008
N° of previous hospital admissions	0.106	0.06	4.505	1.11	1.01-1.23	0.034
High childhood trauma severity (CTQ)	0.06	0.02	8.2	1.06	1.02-1.11	0.004
Constant	-4.664	0.01	16.141	0.01	0.00-0.09	< 0.001

χ^2: 17.974, *P* < 0.001, D.f. = 1; Nagelkerke R^2: 0.33. CTQ: Childhood Trauma Questionnaire.

childhood trauma, the severity of nicotine dependence, and the number of previous hospital admissions. These results partially agree with our initial hypothesis as no association was found with some of the factors previously related with major depression, such as: Personal and familiar antecedents of psychiatric disorders (*e.g.*, suicide attempts, addictions), pain perception, a worse score of functionality, and a lower resilience level. To the best of our knowledge, only one study reported risk factors associated with depression in patients with CVD[30]. However, no study evaluated such a vast array of epidemiological, clinical and psychological factors associated with depression in patients hospitalized with CVD.

Our results should be regarded considering a few issues. First, our study has a cross-sectional design and, as such, hinders the evaluation of causality between the factors evaluated and major depression. Second, our sample included patients with different types of CVD. We have grouped the distinct disorders in a unique group as they share common risk factors and etiological mechanisms associated with inflammatory processes; previous studies have adopted this same strategy[30]. Finally, we have not been able to assess the severity of CVD with an objective measure within this study.

Our sample presented a rate of 27.7% of patients screening positive for depression. This result is comparable with previous studies, which reported a prevalence of

13.5% to 47% of major depression in inpatients with CVD[16,30-33]. Different from previous studies, that reported only 5% of patients with CVD and depression were being treated with antidepressants[33], in our sample, 23.7% of the subjects were taking an antidepressant.

Stressful experiences during the lifespan have been associated with CVD[34] and depression[35]. Childhood trauma is one of the most significant predictors of health problems, life expectancy, psychiatric disorders and the severity of clinical diseases' courses[36]. The occurrence of childhood trauma can influence the development of CVD through changes in metabolic, cardiovascular risk factors like dyslipidemia, central obesity, and hyperglycemia. A Dutch cohort study found that among the childhood trauma subtypes and personality traits, sexual abuse was the primary factor that correlated negatively with serum cholesterol and abdominal circumference measurements[37]. Recurrent stressful events may induce a subtle chronic inflammatory response, enough to contribute to the progression of atherosclerosis and increased the risk of developing CAD[38]. Our results highlight the importance of the assessment of childhood trauma in patients with CVD, as the severity of trauma may predict depression in this population. Clinicians must consider that one possible mechanism of the association between childhood trauma, depression and CVD is the disruption of the key stress-response system, such as the catecholamine system, the hypothalamic-pituitary-adrenal axis, and neurotrophic factors, in early stages of child development. The impairment of the stress response system can influence arousal and emotional behaviour and contribute to increase the allostatic load, impairing brain development and increasing the risk for psychopathology[36].

As reported in the paper of Caro *et al*[30], our results point that nicotine dependence is associated with a positive screening for depression in CVD inpatients. Nicotine dependence is more prevalent in individuals with depression, possibly because these subjects are less prone to engage in smoking cessation programs[9] and tend to use nicotine to alleviate anxiety and dysphoria[39]. As other risk factors for CVD, cigarette use has been associated with damage of the arterial wall. Moreover, the intensification of cigarette use maintains inflammatory response, like chronic stress, and increases risk for depression and CVD[2]. Also, both depression and CVD increase the systemic pro-inflammatory state[2,7], aggravating the pathophysiological mechanisms related to CVD and closing a vicious cycle[38].

Presenting a greater number of previous hospital admissions was another factor associated with positive screening for depression in our study. These results agree with previous findings regarding inpatients with several medical illnesses[32]. Compared to those without depression, medical inpatients suffering from depression have longer hospital stays and higher readmission rates. Both factors underline the burden of this affective disorder among CVD patients, including the financial burden[12,40]. Moreover, each hospital admission can represent an acute stressor for those who experience

it, raising negative feelings about an individual's current health state and prognosis, augmenting depressive symptoms. In the same manner, a higher number of hospitalizations may represent a proxy for CVD severity. Other CVD severity measures were significantly associated with depression in inpatients, namely having an implantable cardioverter defibrillator or being in functional class III or IV[33].

How can we link these three factors to CVD and major depression? In our view, either childhood trauma, nicotine dependence and the number of previous hospitalizations have been associated with stress arousal and pro-inflammatory states. Both conditions are well-known risk factors for major depression and CVD[36].

Our results demonstrate that inpatients presenting both CVD and a positive screening for major depression are more prone to have antecedents of childhood trauma, nicotine dependence and a higher number of previous hospitalizations. Clinicians may consider these factors in the assessment of CVD inpatients at risk for major depression. This measure can improve their treatment approach and patients' prognoses.

ACKNOWLEDGMENTS

COMMENTS

Background
The prevalence of depression is considerably higher among individuals with cardiovascular diseases (CVD) when compared to the general population. Both major depression and depressive symptoms are predictors of poor outcome in patients with CVD. Depressive disorder is frequently overlooked and untreated in individuals with CVD.

Innovations and breakthroughs
This study assessed the influence of the factors associated with positive screening for depression in a sample of patients with CVD hospitalized in a university hospital. After multiple comparisons, the authors found that positive screening for depression was significantly associated with childhood trauma, the severity of nicotine dependence, and the number of previous hospital admissions.

Applications
The results demonstrate that inpatients presenting both CVD and a positive screening for major depression are more prone to have antecedents of childhood trauma, nicotine dependence and a higher number of previous hospitalizations. Clinicians may consider these factors in the assessment of CVD inpatients at risk for major depression. This measure can improve their treatment approach and patients' prognoses.

Peer-review
This is a cross-sectional survey of risk factors associated with depression in patients hospitalized in non-surgical wards and suffering in cardiovascular disease. As both cardiovascular diseases and depression are frequent and possessing a great burden on the family and the society, the study is relevant and interesting.

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