

## INVESTIGACIÓN ORIGINAL

DOI: <http://dx.doi.org/10.15446/revfacmed.v63n3.50860>**Association of depression and stress in acute myocardial infarction: a case-control study***La relación de la depresión y el estrés con el infarto del miocardio: un estudio de casos y controles*Patricia RM Goldfeld<sup>1</sup> • Luciana S. Soares<sup>2</sup> • Waldomiro C. Manfro<sup>3</sup>

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## | Summary |

**Background.** Psychosocial factors have been reported to be independently associated with coronary artery disease (CAD). However the stress variable is still sub detailed and there are few studies that used coronary angiography (CA) to assess CAD.

**Objectives.** To compare levels of depression, stress and stressful life events in three groups of individuals: post-MI (Myocardial Infarction) patients; patients presenting symptoms and no previous MI who underwent cardiac catheterization and had non-significant obstructive CAD and individuals with no symptoms of cardiac disease or others diseases.

**Methods.** We conducted a case-control study, with two cases groups and one control group. The study included 105 patients with recent Myocardial Infarction (MI group), 101 patients with cardiac symptoms and normal CA (CS group), and 100 patients without symptoms of disease (NS group). Multivariate logistic regression was used to assess stress and vital events with an Odds Ratio of 95% confidence interval (CI), controlling for age, sex, education level, income, social support group, Body Mass Index (BMI), sedentary lifestyle and family history of MI or sudden death.

**Results.** MI patients group showed depression with an OR=4.47(95% CI, 2.36 to 8.46,  $p<.001$ ), and stress OR=5.37(95% CI, 2.94–9.78,  $p<.001$ ) whereas CS group showed depression: OR=6.95(95% CI, 3.64–13.28,  $p<.001$ ) and stress: OR=9.18 (95% CI, 4.73–17.82,  $p<.001$ ) compared to patients without symptoms. After adjusting the groups for the following risk factors: age,

sex, education, income, social support, obesity, sedentary lifestyle, family history of MI or sudden death, the OR showed the following variation: in the MI group, depression OR=2.51 (95% CI, 1.05 to 5.98,  $p=.038$ ), stress, OR=8.76(95% CI, 3.48 to 22.01,  $p<.001$ ), while the CS group showed: depression OR=3.25(95% CI, 1.40–7.55,  $p<.01$ ) and stress OR=12.24 (95% CI, 4.81–31.14,  $p<.001$ ). The raised effect of variable stress after adjustment was promoted by age, sex and physical inactivity variables, and did not affect the significance level ( $p<.001$ ).

**Conclusions.** This study has demonstrated that subjects with cardiac symptoms without overt CAD show similar depression and/or stress levels than post-MI patients, and that post-MI patients and CS patients experience more stress and depression than control patients, even when they adjusted in terms of age, sex, education level, family income, social support, obesity, sedentary lifestyle and family history of MI and / or sudden death.

**Keywords:** Depression; Stress; Infarction; Cardiovascular Disease; Risk factors; Epidemiology. (MeSH)

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## Resumen

**Antecedentes.** Factores psicosociales han demostrado asociación independiente con la enfermedad arterial coronaria

(EAC); sin embargo, la variable estrés sigue siendo sub detallada y hay pocos estudios que utilizaron la angiografía coronaria (CA) para evaluar EAC.

**Objetivos.** Comparar los niveles de depresión, el estrés y los acontecimientos vitales estresantes en tres grupos de personas: en pacientes post-IM (infarto de miocardio), en pacientes que presentan síntomas cardíacos y cateterismo cardíaco normal y en individuos sin síntomas de enfermedades cardíacas.

**Métodos.** Se realizó un estudio de casos y controles —dos grupos de casos y un grupo control—. El estudio incluyó a 105 pacientes con infarto de miocardio reciente (grupo MI), 101 pacientes con síntomas cardíacos y CA normal (grupo CS), y 100 pacientes sin síntomas de la enfermedad (grupo NS). Se utilizó multivariante de regresión logística para evaluar el estrés y los acontecimientos vitales con una odds ratio de intervalo de confianza del 95% (IC), controlando por edad, sexo, nivel educativo, ingresos, grupo de apoyo social, el índice de masa corporal (IMC), el sedentarismo y los antecedentes familiares de infarto de miocardio o muerte súbita.

**Resultados.** Los pacientes del grupo MI mostraron depresión con una OR=4.47 (IC del 95%, 02:36-08:46,  $p<0.001$ ), y el estrés OR=5.37 (IC 95%, 2.94-9.78;  $p<0.001$ ) mientras que el grupo CS mostró depresión OR=6.95 (95% CI, 3.64 a 13.28,  $p<0.001$ ) y el estrés OR=9.18 (95% CI, 4.73 a 17.82,  $p<0.001$ ) en comparación con los pacientes sin síntomas. Después de ajustar por factores de riesgo: edad, sexo, educación, ingresos, apoyo social, obesidad, sedentarismo, antecedentes familiares de infarto de miocardio o muerte súbita, el OR mostró la siguiente variación: en el grupo de MI, depresión OR=2.51 (IC del 95%, 1.05 a 5.98,  $p=0.038$ ), el estrés, OR=8.76 (IC del 95%, 3.48–22.01,  $p<0.001$ ), y CS grupo, depresión OR=3.25 (95% CI, 1.40 a 7.55,  $p<0.01$ ) y el estrés OR=12.24 (95%, IC, 4.81 a 31.14,  $p<0.001$ ). El efecto de elevación de la variable estrés después del ajuste fue promovida por las variables de edad, sexo e inactividad física, y no afectó el nivel de significación ( $p<0.001$ ).

**Conclusiones.** Este estudio ha demostrado que los sujetos con síntomas cardíacos sin EAC presentan similares niveles de depresión y / o estrés a los de los pacientes post-IM. También se demostró que los pacientes post-IM y los pacientes CS tienen más estrés y depresión que los controles, incluso cuando se ajustan por edad, sexo, nivel de educación, ingreso familiar, apoyo social, obesidad, sedentarismo y antecedentes familiares de infarto de miocardio y / o muerte súbita.

**Palabras clave:** Depresión; Infarto del miocardio; Factores de riesgo; Epidemiología (Desc).

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## Introduction

Heart disease (1,2) and depression (3) affect a significant number of individuals worldwide annually and the effective treatment of these patients has an important public health impact.

Studies have estimated that 20 to 45% of post-MI patients have some symptoms of depression (4). Acute depressive reactions have also been implicated as triggers of acute coronary syndromes (5). The presence of depression in patients with pre-existing cardiovascular disease is a risk factor for recurrence of cardiovascular events and death (6-8).

The relationship between depression and cardiovascular disease is complex and bidirectional (9) and as well as depression may influence CAD, chronic diseases can also lead to depressive symptoms. Even sub threshold depressive symptoms that do not meet the criteria for a diagnosis of major depressive disorders are risk factors for the development of CHD events in healthy patients (10). On the other hand, chest pain is a common symptom in cardiology emergency rooms and after a diagnostic evaluation (11) only 15-25% of these patients have been diagnosed an acute coronary artery syndrome.

The stress variable shares some psycho-physiological (12) pathways with depression, and may be implicated in the relationship between depression and CAD. The naturalistic studies on natural disasters (stressful life events) are evidence that significant stress levels can precipitate acute cardiovascular events, but studies have also shown chronic stress associated with CAD.

Scientific literature presents several studies using standardized instruments in search of the variable stress, however research with large samples does not allow studies using instruments with qualitative design, more suitable in studies with smaller samples. The same goes for expensive and invasive tests such as cardio angiography.

The present study aimed to compare symptoms of depression, stress and vital events in recent MI subjects with subjects who have cardiovascular symptoms, but without overt coronary artery disease, and with another group of subjects without symptoms of disease.

## Methods

This study was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre, Universidade Federal

do Rio Grande do Sul, Brazil, and consisted of a case-control study with two groups of incident cases and a control group. All the subjects completed an informed consent form. Data collection was performed in a protected environment by people trained to implement the specific research protocol.

### Study subjects

Study participants were recruited via consecutive sampling in the Cardiovascular Catheterization Laboratory. The MI (13) cases and those with symptoms but no previous MI were selected among patients undergoing cardiac catheterization, the control group consisted of individuals without symptoms of any disease and was obtained through family and friends of patients undergoing cardiac catheterization, in the same service (the assessor blind to the factor under study). In order to be chosen, MI cases were eligible if they had had in the past month history of anginal symptoms, ECG changes or enzymes elevation indicative of MI. Five individuals in the control group and two cases refused to participate in the study while eighteen were excluded after data collection, due to their exclusion criteria.

### Procedures

*Inclusion criteria.* In the MI group were included individuals with clinical, laboratory and/or electrocardiographic MI reported within 30 days of collection. In the group with cardiac symptoms, individuals presenting symptoms and no previous MI, who underwent cardiac catheterization (14) and had non significant obstructive CAD were included. Control group included those with no symptoms of cardiac disease or other diseases.

*Exclusion criteria.* In the MI group and in the CS group, patients with valvular heart disease, cardiac shock, cardiomyopathy (including Takotsubo (15)), angina, coronary artery bypass grafting in the last ninety days, stroke and severe infection in the last 180 days were excluded. In the control group (NS), patients with diseases of any kind were excluded.

*Instruments.* Structured questionnaires were administered by trained staff in the same way in all three groups. Personal data such as sex, age, race, origin, marital status, financial, education, professional status, degree of social contact, medical history, tobacco and alcohol use, information on menopausal status in women, level of physical activity, family history of cardiovascular disease, diabetes mellitus, hypertension, dyslipidemia and sudden death were asked.

We collected measures of height and weight, waist circumference (measured at the midpoint between the iliac

crest and last rib), body-mass index, arterial blood pressure, ECG and results of coronary angiography were also obtained. Those individuals who showed a degree of stenosis equal or less than 50% at visual (14) analysis on angiography were considered free of CAD.

To assess depression symptoms we used the Beck Depression Inventory (BDI) (16). This self-assessment scale with 21 items is one of the most widely used, both in research and in clinical practice, it has been translated into several languages and validated (17) in the country of research. For this survey, 12 was considered the cutoff for mild depression as validation.

Stress was assessed by the Lipp Inventory of Stress Symptoms for adults (ISSL) (18), a qualitative-quantitative scale, with a four phases model, based on the three phases Selye's model, and that comprehends the stages of alarm, resistance, near-exhaustion and exhaustion. It also evaluates the predominance of somatic and / or psychological domain.

To evaluate the stress caused by external events in the last year, the Social Readjustment Rating Scale (SRRS) (19), one of the most used to measure life events, was chosen.

Sample calculation was performed to detect a difference of 4% between groups, resulting in 100 subjects per group according to a power of 90%.

### Statistical analysis

Variable frequency tables were compiled with number and percentage for categorical variables. Mean and standard deviation were calculated for continuous variables and compared by t-test for the presence or absence of depression, or ANOVA for the three groups (control cases). For categorical variables, chi-square or Fisher's test was used. For the significant variables ( $p < .05$ ) in relation to outcome groups, multinomial logistic regression unadjusted calculation was performed, followed by multivariate analysis, including the variables: age, sex, education level, monthly income, BMI, physical inactivity, family history of MI / sudden death, depression and stress.

### Results

Baseline and demographic characteristics of three groups are summarized in Table 1. In the MI group, all individuals reported only one MI previous history, 53 were treated with coronary angioplasty with stent implantation and only one subject had been submitted to two previous angioplasties.

**Table 1.** Population characteristics and risk factors.

| Variables                                                |                       | MI group(105)            | CS group(101)            | NS group(100)          | P                  |
|----------------------------------------------------------|-----------------------|--------------------------|--------------------------|------------------------|--------------------|
| Sex (masc)                                               |                       | 65 <sub>a</sub> (61.9)   | 38 <sub>b</sub> (37.6)   | 34 <sub>b</sub> (34)   | <.001              |
| Age                                                      |                       | 60.63±10.56              | 57.58±10.67              | 49.15±9.49             | <.001 <sup>†</sup> |
| Level of Education                                       | Incomplete Elementary | 43 <sub>c</sub> (41.0)   | 66 <sub>d</sub> (65.3)   | 28 <sub>c</sub> (28.0) | <.001              |
|                                                          | Elementary and above  | 62 <sub>e</sub> (59.0)   | 35 <sub>f</sub> (34.7)   | 72 <sub>e</sub> (72.0) |                    |
| Race                                                     | White                 | 90(85.7)                 | 82(81.2)                 | 87(87.0)               | .485               |
|                                                          | Black/mixed race      | 15(14.3)                 | 19(18.8)                 | 13(13.0)               |                    |
| Marital Status                                           | Married               | 66(62.9)                 | 66(65.3)                 | 79(79.0)               | .028               |
|                                                          | Single/Div./Widow     | 39(37.1)                 | 35(34.7)                 | 21(21.0)               |                    |
| Professional State                                       | Active                | 46 <sub>g</sub> (43.8)   | 31 <sub>g</sub> (30.7)   | 80 <sub>h</sub> (80.0) | <.001              |
|                                                          | Inactive              | 59 <sub>i</sub> (56.2)   | 70 <sub>i</sub> (69.3)   | 20 <sub>j</sub> (20.0) |                    |
| Monthly family Income<br>(according to the minimum wage) | Up to 1               | 9 <sub>k</sub> (8.8)     | 14 <sub>k</sub> (14.7)   | 1 <sub>l</sub> (1.0)   | <.001              |
|                                                          | From 1.1 to 3         | 36 <sub>m</sub> (35.3)   | 49 <sub>n</sub> (51.6)   | 34 <sub>m</sub> (34.3) |                    |
|                                                          | From 3.1 to 5         | 30 <sub>o,p</sub> (29.4) | 19 <sub>o</sub> (20.0)   | 34 <sub>p</sub> (34.3) |                    |
|                                                          | >5                    | 27 <sub>q</sub> (26.5)   | 13 <sub>r</sub> (13.7)   | 30 <sub>q</sub> (30.3) |                    |
| Residential Accompaniment                                | Lives alone           | 16(15.2)                 | 14(13.9)                 | 7(7.0)                 | .161               |
|                                                          | With one person       | 32(30.5)                 | 28(27.7)                 | 23(23.0)               |                    |
|                                                          | With more than one    | 57(54.3)                 | 59(58.4)                 | 70(70.0)               |                    |
| Low social support                                       |                       | 76 <sub>s</sub> (72.4)   | 69 <sub>s,t</sub> (68.3) | 56 <sub>t</sub> (56.0) | .038               |
| BMI                                                      |                       | 26.65±4.16               | 28.35±5.66               | 25.94±3.36             | .001               |
| Hypercholesterolemia                                     |                       | 40(38.1)                 | 33(32.7)                 | 0(0)                   |                    |
| Hypertension                                             |                       | 73(69.5)                 | 76(75.2)                 | 0(0)                   |                    |
| Diabetes Mellitus                                        |                       | 29(27.6)                 | 16(15.8)                 | 0(0)                   |                    |
| Sedentary lifestyle                                      |                       | 89 <sub>u</sub> (84.8)   | 76 <sub>u</sub> (75.2)   | 57 <sub>v</sub> (57.0) | <.001              |
| Current Smoker                                           |                       | 32 (47.1)                | 15(26.8)                 | 23(45.1)               | .049               |
| Former Smoker                                            |                       | 68(64.8)                 | 56(55.4)                 | 51(51.0)               | .121               |
| Alcoholism                                               |                       | 15(14.4)                 | 8(7.9)                   | 9(9.0)                 | .266               |
| Family history of MI                                     |                       | 45(46.4)                 | 31(33.0)                 | 33(33.0)               | .090               |
| Family history of sudden death                           |                       | 41 <sub>w</sub> (40.6)   | 22 <sub>x</sub> (22.2)   | 22 <sub>x</sub> (22.2) | .004               |
| Family history of angina                                 |                       | 51(53.7)                 | 54(58.1)                 | 47(50.0)               | .542               |

MI group: patients with previous myocardial infarction; CS group: patients with cardiac symptoms and normal coronary angiography; NS: control group. Categorical variables: Number/Percentage; continuous variables: Mean±SD, variables in rows and groups in columns. Equal letters in lines: No significant differences among groups; Different letters in lines: Significant differences between groups. † ANOVA between groups with Turkey adjustments; All other comparisons=Chi-square test.

Table 2 shows the groups distribution according to precordial pain. In the MI group, 57.2% had chest pain, 54.5% of these had chest pain as their only symptom, and 36.2% were asymptomatic.

The others reported fatigue, dyspnea and/or palpitations associated. In the CS group, 80% of patients showed chest pain, and 55% of these had chest pain as their only symptom.

**Table 2.** Precordial pain results in the three groups

| Precordial Pain | MI group(105)          | CS group(101)          | NS group(100)          | P     |
|-----------------|------------------------|------------------------|------------------------|-------|
| Yes             | 60 <sub>a</sub> (42.6) | 81 <sub>b</sub> (57.4) | 0 <sub>c</sub> (0)     | <.001 |
| No              | 45 <sub>d</sub> (42.6) | 20 <sub>e</sub> (30.8) | 100 <sub>f</sub> (100) |       |

MI group: patients with previous myocardial infarction; CS group: patients with cardiac symptoms and normal coronary angiography; NS: control group. Different letters in lines: Significant differences among groups. Chi-square test.

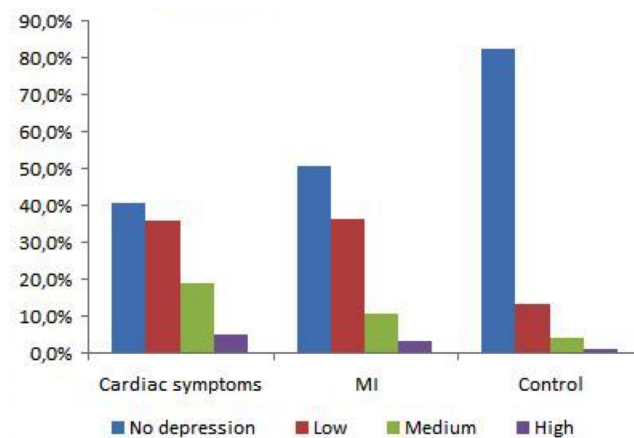
Table 3 shows the distribution of subjects according to depression (BDI), stress (ISSL) and Vital Events (SRRS) levels in the three groups.

**Table 3.** Depression, Stress and Vital Events results in the three groups

| Variables           | MI group(105)          | CS group(101)          | NS group(100)        | P                  |
|---------------------|------------------------|------------------------|----------------------|--------------------|
| Depression (BDI)    | 12.46±8.43             | 14.83±9.59             | 6.84±7.18            | <.001 <sup>†</sup> |
| Stress (ISSL)       | 78 <sub>c</sub> (74.3) | 84 <sub>c</sub> (83.2) | 35 <sub>d</sub> (35) | <.001              |
| Vital Events (SRRS) | 204.80±121.71          | 212.31±102.92          | 201.73±94.96         | .766 <sup>†</sup>  |

MI group: patients with previous myocardial infarction; CS group: patients with cardiac symptoms and normal coronary angiography; NS: control group. Equal letters in lines: No significant differences among groups; Different letters in lines: Significant differences among groups. † ANOVA between groups with Turkey adjustments; Chi-square test. BDI=Beck Depression Inventory, ISSL=Lipp Inventory of Stress Symptoms for adults, SRRS=Social Readjustment Rating Scale.

Figure 1 describes the distribution of BDI depression levels according to the three groups.



**Figure 1.** Bar graph with levels of depression (BDI) between groups. No depression=BDI levels from zero to 11; Low=from 12 to 19; Medium=from 20 to 35 and High=from 36 to 63.

The main results of the ISSL, on the characteristics of the three groups compared to the stress phases, can be found in Table 4.

**Table 4.** Levels of stress between groups.

|                 | MI (n=105)             | With Symptoms(n=101)   | Controls(n=100)        | Total     | P     |
|-----------------|------------------------|------------------------|------------------------|-----------|-------|
|                 |                        |                        |                        |           | <.001 |
| No stress       | 27 <sub>a</sub> (25.7) | 17 <sub>a</sub> (16.8) | 65 <sub>b</sub> (65.0) | 109(35.6) |       |
| Alert           | 4 <sub>c</sub> (3.8)   | 6 <sub>c</sub> (5.9)   | 0 <sub>d</sub>         | 10(3.3)   |       |
| Resist          | 55 <sub>e</sub> (52.4) | 57 <sub>e</sub> (56.4) | 33 <sub>f</sub> (33.0) | 145(47.4) |       |
| Near-exhaustion | 14 <sub>g</sub> (13.3) | 18 <sub>g</sub> (17.8) | 2 <sub>h</sub> (2.0)   | 34(11.1)  |       |
| Exhaustion      | 5 <sub>i</sub> (4.8)   | 3 <sub>i</sub> (3.0)   | 0 <sub>j</sub>         | 8(2.6)    |       |

Number and percentage; Chi-square test. Equal letters in lines: No significant differences among groups; Different letters in lines: Significant differences among groups.

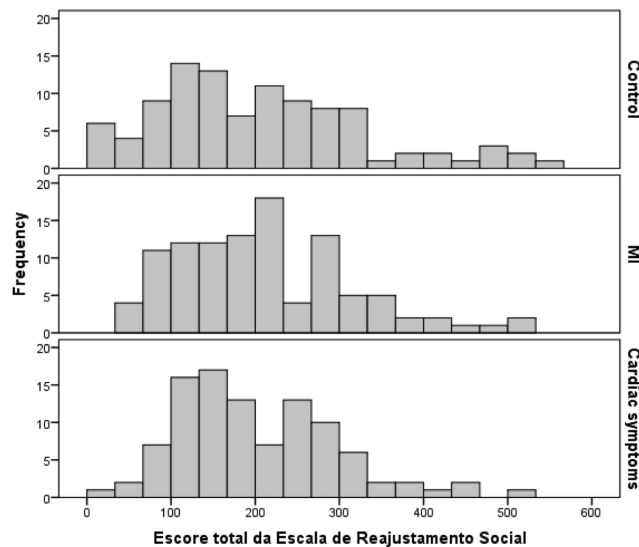
The results related to the prevalence of somatic and/or psychological fields in the three groups are shown in Table 5.

**Table 5.** Prevalence of somatic and/or psychological fields.

|               | MI (n=105)             | With Symptoms(n=101)   | Controls(n=100)        | Total     | P     |
|---------------|------------------------|------------------------|------------------------|-----------|-------|
|               |                        |                        |                        |           | <.001 |
| No stress     | 27 <sub>a</sub> (25.7) | 17 <sub>a</sub> (16.8) | 65 <sub>b</sub> (65.0) | 109(35.6) |       |
| Physical      | 14 <sub>c</sub> (13.3) | 28 <sub>d</sub> (27.7) | 4 <sub>e</sub> (4.0)   | 46(15.0)  |       |
| Psychological | 61 <sub>f</sub> (58.1) | 52 <sub>f</sub> (51.5) | 31 <sub>g</sub> (31.0) | 144(47.1) |       |
| Both          | 3 <sub>h,i</sub> (2.9) | 4 <sub>h</sub> (4.0)   | 0 <sub>i</sub>         | 7(2.3)    |       |

Number and percentage; Chi-square test. Equal letters in lines: No significant differences among groups; Different letters in lines: Significant Differences among groups.

The SRRS showed no differences between groups in the relationship of vital events. Figure 2 shows bar graphs of vital events total frequency (SRRS) in the three groups of subjects.



**Figure 2.** Bar graph with frequency of Vital Events (SRRS) for the three groups of subjects.

Table 6 shows the Multinomial Logistic Regression unadjusted and adjusted results.

**Table 6.** Multinomial Logistic Regression unadjusted and adjusted.

| Risk Factor                     | Group | OR (95% IC)        | P     | OR ad(95% IC)     | P     |
|---------------------------------|-------|--------------------|-------|-------------------|-------|
| Age                             | A     | 2.22 (1.19-4.15)   | .012  | 1.35(1.09-1.19)   | <.001 |
|                                 | B     | 2.00(1.60-3.75)    | .032  | 1.09(1.05-1.14)   | <.001 |
| Sex                             | A     | 3.15 (1.78-5.59)   | <.001 | 7.51(3.14-17.95)  | <.001 |
|                                 | B     | 1.17(.66-2.09)     | .592  | 3.48(1.45-8.39)   | <.01  |
| Elementary education Incomplete | A     | 1.78(.99-3.20)     | .052  | .67(.27-1.62)     | .369  |
|                                 | B     | 4.85(2.66-8.82)    | <.001 | 1.52(.63-3.65)    | .353  |
| Very low monthly income         | A     | 10.00(1.19-84.18)  | .034  | 2.15(.79-5.85)    | .134  |
|                                 | B     | 32.31(3.84-272.02) | .001  | 4.56(1.59-13.13)  | <.01  |
| Low monthly income              | A     | 1.18(.58-2.37)     | .649  | 1.89(.69-5.19)    | .215  |
|                                 | B     | 3.33(1.52-7.29)    | .003  | 2.31(.76-7.00)    | .139  |
| Low social support              | A     | 2.06(1.15-3.69)    | <.05  | 2.62(1.15-5.96)   | <.05  |
|                                 | B     | 1.48(.84-2.62)     | .176  | 1.75(.79-3.89)    | .170  |
| Family risk of MI and SD        | A     | 1.87(1.07-3.29)    | .029  | 1.47(.66-3.27)    | .346  |
|                                 | B     | 1.01(.57-1.79)     | .968  | .71(.32-1.58)     | .396  |
| BMI                             | A     | .97(.45-2.10)      | .930  | .75(.28-2.05)     | .577  |
|                                 | B     | 2.28(1.14-4.59)    | .020  | .39(1.51-1.00)    | .049  |
| Sedentary lifestyle             | A     | 4.20(2.16-8.15)    | <.001 | 2.28(.91-5.67)    | .079  |
|                                 | B     | 2.29(1.26-4.18)    | <.01  | 1.04(.44-2.43)    | .932  |
| BDI-Depression                  | A     | 4.47(2.36-8.46)    | <.001 | 2.51(1.05-5.98)   | .038  |
|                                 | B     | 6.95(3.64-13.28)   | <.001 | 3.25(1.40-7.55)   | <.01  |
| ISSL-Stress                     | A     | 5.37(2.94-9.78)    | <.001 | 8.76(3.48-22.01)  | <.001 |
|                                 | B     | 9.18(4.73-17.82)   | <.001 | 12.24(4.81-31.14) | <.001 |

Reference: control group. Group A: MI, Group B: Cardiovascular Symptoms without CAD. SD=sudden death; BMI=Body Mass Index; BDI=Beck Depression Inventory; ISSL=Lipp Inventory of Stress Symptoms for adults.

## Discussion

Our study shows that patients with cardiovascular symptoms without overt coronary artery disease have similar chances of depression and stress than post-MI patients. And that both groups have a greater chance of depression and stress than the control group patients. These depression and stress chances remain significant even when they were adjusted for confounders variables such as age, sex, education levels, family income, social support, obesity, sedentary lifestyle and family history of MI and/or sudden death.

We found, after adjustment, a decreased chance of depression ORMI=4:47 to 2:51 and ORCS=6.95 to 3.25, and a increases chance of stress, ORMI=5:37 to 8.76 and ORCS=9.18 to 12.24. Depression showed a reduction of the OR because of the role of other risk factors in the outcome of MI or symptoms. The variables one by one analysis with the stress variable by Logistic Regression showed the increase of stress when the age, sex and sedentary variables were controlled, without variation of the level of significance. This variation may be explained by group differences in age, sex and sedentary, that pulled down the stress variable when the unadjusted analysis was performed.

Rona et al. (20), in a longitudinal study, assessed which baseline risk factors are associated with persistent and partially remitted Post Traumatic Stress Disorder (PTSD) in comparison to fully remitted PTSD, and it was found that older age variable increased the number of events reported ( $p<.05$ ). Marcellini et al. (21) found that lower scores of physical activity were associated to higher scores of Geriatric Depression Scale ( $r=-0.425$ ;  $p<0.01$ ), lower scores of Mini Mental State Examination ( $r=0.266$ ;  $p<0.001$ ) and higher score of Perceived Stress Scale ( $r=-0.131$ ;  $p<0.05$ ).

The present study analyzed a group of patients with cardiac symptoms without overt CAD, it complements what Rugulies (22) says about that one might think that both depression and future coronary events could be caused by sub-clinical manifestations and not a diagnosed cardiovascular disease. However, he said controlled studies for this potential bias of confusion (a medical intensive early cardiovascular disease and / or exclusion of events during the first year of follow up) showed only a small relative risk reduction of 1, 77 to 1.51, which remained significant.

Most studies on depression and CAD are follow-up evaluations, with depressive patients without CAD at base, to assess the incidence of CAD, or about patients with depression after MI, to assess the incidence of cardiovascular events. Our study is more like the design of the INTERHEART (23) study, but with a small sample, with the idea of trying to deepen the study of these individuals.

In the INTERHEART (23) study, the stress is measured post-MI with 4 questions and shows an OR from 1.33 (financial) to 2.17 (continuous), and depression OR=1.55. Our study used a qualitative-quantitative scale and found a stress post-MI adjusted OR=8.76. On the scientific literature, we found only in SHEEP (24) study an OR of stress at work with a level that was closest to our study, OR=6.0.

A systematic review of Von Känel (25), psychosocial factors with CHD occur at levels higher than would occur by chance: 40% of CAD patients have some form of relevant depression, and in the general population it appears in 5–10% of individuals. In our study, depression occurred in 49.5% in post-MI, 60.0% in subjects without CHD symptoms, and 18% in the control group, and stress, MI=74.3%, CS=83.2% and control group=35%.

Our study agreed with Von Känel (25) that in the same cardiac patient, psychosocial factors may co-occur, such as depression and low social support or job stress and exhaustion. In our study, we found co-occurrence of stress, depression, low social support.

The higher prevalence of stress was in the level of resistance and in the psychological field. The CS group showed a higher rate of somatic symptoms than other groups and this seems to indicate a tendency to somatization by these individuals without coronary disease base.

In the stress area is important to evaluate the external factors, which are vital events and social support, beyond the adaptive capacities of the individual (coping skills). In our study, we did not find differences in life events between the three groups. Regarding this, our findings agree with those from the SHEEP (24), Twisk et al. (26) and Copenhagen City Heart (27) studies, who found no differences in life events. However, our study disagrees with the INTERHEART study (23), that found an OR=1.48 for stressful life events in MI cases. Rafanelli et al. (28) also found more events ( $p<.001$ ), in a case-control study of patients with post-MI and unstable angina, and depression in 39.2% of cases. According to Tennant (29), assessment of life events is based on a series of methodological problems because the reliability and validity of measures are not entirely satisfactory.

Regarding social support, we found that the MI group had less social support groups with OR=2.62 (95%CI, 1.15–5.96,  $p<.05$ ) and that NS group had more social support, like family and friends ( $p<.01$ ). These results agree with those from Pignalberi et al. (31) study, where heart patients showed significantly more social isolation ( $p<.05$ ).

Another important finding of our study is that precordial pain is the most frequent symptom in both groups of patients, but is more frequent in those with normal coronary arteries. The studies found in the literature search show conditions with organic bases, and we did not found studies with no organic base.

The MI group showed more male subjects than the CS group and the control group. There was more chance of being male in the MI group and after adjustment, the odds greatly increased in both groups of patients and became significant also for the CS group. According to Framingham study (31), the male subjects have more chance OR=1.73 for MI than females. This study found the 30-year hard event rates adjusted were 7.6% for women and 18.3% for men.

The two groups of patients had a higher average age. The OR became more significant after adjustment. These results also agree with those of Framingham (31), OR=2.09, which showed more chance for older individuals to present MI.

CS group showed lower educational level. The OR was significant for CS group and lost significance after adjustment.

Our findings in this area are different from INTERHEART (32), that found low levels of education were more common in cases compared to the control group, with  $OR=1.31$ ,  $p < 0.0001$ . They found low education was globally the most consistent marker associated with increased risk for MI, most predominant in high-income countries.

The MI group had more patients with family history of sudden death ( $< .01$ ). In INTERHEART's findings (33), both maternal and paternal histories of MI were associated with Increased MI risk, with  $OR=1.74$ .

### Study limitations

The present study has no conflicts of interest. However some methodological bias must be considered, like demographic differences between the control group and the two patient groups. About recruiting subjects with similar ages, according to a study (34) performed in the same hemodynamic service, MI was the first manifestation of ischemic heart disease in 49% of the patients. As the present study aimed to compare the two patient groups with a healthy subjects group, if we had recruited older individuals, we would have more chance to have subjects with silent DAC among them. These sample differences were controlled by the statistical model.

It should also be considered that the two case group subjects had undergone a coronary angiography, which could influence stress and depression. To control this factor, the BDI assesses depression in the previous week and the ISSL scale assesses stress in the previous month, and not just at the time of assessment. Furthermore, the results showed the ISSL prevalence of the resistance stage of stress. According to Lipp (35), for a subject to reach the resistance stage of stress, it needs to be continued, leading to be worn out and exhausted or tired with memory difficulties. Other risk factors could be potential confounders controlled by the statistical model. We were unable to control risk factors like diabetes, hypercholesterolemia or hypertension that have been variables due to exclusion in the control group.

### Conclusions

In conclusion, our study demonstrated that subjects with cardiac symptoms, without overt CAD, have similar stress and depression symptoms than post-MI patients. The study has also found that MI patients and CS patients have more stress and depression than controls, even when adjusted for age, sex, education level, family income, social support, obesity, sedentary lifestyle and family history of MI and/or sudden death.

This study raises important precedents, nevertheless prospective studies with diagnoses of depressive disorders and stress assessment and cardiovascular outcomes are still needed.

### Conflicts of interest

No conflict of interest stated by the authors.

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