

# Female Psychological Adjustment Following an Acute Coronary Syndrome

## Adaptação Psicológica nas Mulheres Após Síndrome Coronária Aguda



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### ABSTRACT

**Introduction:** The outcomes of cardiovascular disease are consistently worse among women, regardless of age or disease severity. Such trend might arise from psychosocial factors, which should be examined in this population.

**Objective:** To evaluate the influence of type-D personality on anxiety and depression symptoms reported by female patients after a first acute coronary syndrome.

**Material and Methods:** As part of a larger study, 34 female patients with a first acute coronary syndrome were compared with 43 controls on psychosocial measures (Hospital Anxiety and Depression Scale; type-D personality, DS - 14).

**Results:** Hypertension ( $p < 0.001$ ), diabetes ( $p < 0.05$ ), dyslipidemia ( $p < 0.05$ ), type-D personality ( $p = 0.001$ ) and anxiety ( $p < 0.001$ ) were more prevalent among patients. Exercise ( $p < 0.05$ ) and antidepressant use ( $p < 0.05$ ) were more common among controls. Logistic regression analysis confirmed that higher prevalence of hypertension ( $p < 0.05$ ), dyslipidemia ( $p < 0.05$ ), type-D personality ( $p < 0.05$ ), anxiety ( $p < 0.05$ ) and less antidepressant use ( $p < 0.05$ ), were independently associated with acute coronary syndrome. Type-D personality was associated with higher Hospital Anxiety and Depression Scale scores in controls (anxiety:  $p = 0.001$ ; depression:  $p < 0.001$ ) but not in patients.

**Discussion:** High anxiety after an acute coronary syndrome might reflect a short-term adaptive response, albeit worsening the disease long-term prognosis. The lack of differences in some group comparisons (patients *versus* controls for depression scores; type-D 'positive' *versus* type-D 'negative' for anxiety and depression scores within patients) is discussed.

**Conclusion:** Type-D personality, high anxiety, hypertension and dyslipidemia seem to cluster among female acute coronary syndrome patients. Nevertheless, type-D personality itself was not associated with higher anxiety and depressive scores during the post-acute period.

**Keywords:** Acute Coronary Syndrome/psychology; Adaptation, Psychological; Anxiety Disorders; Depressive Disorder; Female

### RESUMO

**Introdução:** As consequências da doença cardiovascular são consistentemente piores em mulheres, independentemente da idade ou gravidade da doença. Esta tendência pode resultar de factores psicossociais que devem ser examinados nesta população.

**Objectivo:** Avaliar a influência da personalidade tipo-D nos sintomas de ansiedade e depressão reportados por mulheres após uma primeira síndrome coronária aguda.

**Material e Métodos:** Como parte de um estudo mais alargado, compararam-se 34 mulheres com uma primeira síndrome coronária aguda com 43 controlos em medidas psicossociais (*Hospital Anxiety and Depression Scale*; Personalidade tipo-D, escala DS - 14).

**Resultados:** Hipertensão ( $p < 0,001$ ), diabetes ( $p < 0,05$ ), dislipidemia ( $p < 0,05$ ), personalidade tipo-D ( $p = 0,001$ ) e ansiedade ( $p < 0,001$ ) foram mais prevalentes nas doentes. A prática de exercício ( $p < 0,05$ ) e a toma de antidepressivos ( $p < 0,05$ ) foram mais comuns entre controlos. A análise de regressão logística confirmou que uma maior prevalência de hipertensão ( $p < 0,05$ ), dislipidemia ( $p < 0,05$ ), personalidade tipo-D ( $p < 0,05$ ), ansiedade ( $p < 0,05$ ) e uma menor utilização de antidepressivos ( $p < 0,05$ ), estavam independentemente associados à síndrome coronária aguda. A personalidade tipo-D associou-se a maiores pontuações *Hospital Anxiety and Depression Scale* nos controlos (ansiedade:  $p = 0,001$ ; depressão:  $p < 0,001$ ), mas não nas doentes.

**Discussão:** Ansiedade elevada após uma síndrome coronária aguda pode traduzir uma resposta adaptativa a curto-prazo, embora agrave o prognóstico da doença a longo-prazo. A ausência de diferenças em algumas comparações (doentes *versus* controlos para pontuações de depressão; tipo-D 'positivos' *versus* tipo-D 'negativos' para pontuações de ansiedade e depressão entre doentes) é discutida.

**Conclusão:** A personalidade tipo-D, ansiedade, hipertensão e dislipidemia parecem associar-se nas doentes com síndrome coronária aguda. Apesar disso, a personalidade tipo-D não se associou a maiores pontuações de ansiedade e depressão no período pós-agudo.

**Palavras-chave:** Perturbação Depressiva; Perturbações de Ansiedade; Mulheres; Síndrome Coronária Aguda/psicologia

### INTRODUCTION

Approximately 55% of all female deaths in Europe are caused by cardiovascular disease (CVD), in particular coronary artery disease and stroke,<sup>1</sup> more than one in five women die because of ischemic heart disease (IHD) and the disability burden is expected to rise concomitantly given

the longer life expectancy of women.<sup>2</sup>

In recent years, gender differences in prevalence rates, symptom profiles and even medical outcomes have accumulated.<sup>1-4</sup> Women with IHD have worse outcomes than men regardless of age<sup>3</sup> and female pathophysiology

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of myocardial ischemia, biochemical and neuro-hormonal factors might combine to place women at a disadvantage.<sup>3</sup> Further, classical biomedical risk factors can have a different relative weight depending on gender<sup>4</sup> and psychosocial factors reliably implicated in the risk and expression of CVD, also present important gender differences.<sup>5-7</sup>

Depressive symptoms have been consistently associated with worse prognosis among CVD patients and self-reported depressive symptoms are independent prognostic factors of cardiac mortality even in the absence of a clinical diagnosis of depression.<sup>8</sup> As in the general population, female CVD patients are twice as likely to experience depression.<sup>9</sup> Depression is also an established risk factor for CVD in the community, increasing both cardiac morbidity and cardiac mortality.<sup>10-12</sup> Similarly, anxiety has also been identified as a risk factor for worse prognosis in cardiac patients<sup>13,14</sup> and is also an independent risk factor for CVD in community samples,<sup>11,14,15</sup> with recent evidence pointing to 20% – 30% increased risk for first acute myocardial infarction (AMI).<sup>11</sup>

Stable personality traits relating to distress have also been implicated in CVD.<sup>16</sup> Type-D (distressed) personality comprises traits of negative affectivity and social inhibition and has been associated with a wide range of adverse health outcomes.<sup>17</sup> Prevalence rates range from 25% to 28% among CVD patients<sup>17</sup> and from 10% to 40% in the general population,<sup>17-21</sup> although studies evaluating type-D personality in women are lacking. Among CVD patients, type-D personality has been associated with an increased risk of both cardiac events and worse outcome.<sup>22,23</sup> In community studies, type-D participants experience high levels of mental distress and poor physical health status.<sup>19</sup> However, it is unknown whether type-D personality influences emotional adjustment responses following a serious cardiac event.

## MATERIAL AND METHODS

### Participants

As part of a larger longitudinal study examining the impact of psychosocial factors in cardiac patients' prognosis, 34 female patients consecutively admitted with a first episode of ACS to the coronary unit of a general hospital in Porto, Portugal, were recruited. In parallel, 43 female controls matched by age were recruited at primary health provision contexts and general practices located in the same Health Administration Region. The study protocol was approved by the Ethics Review Board and written informed consent was obtained from all study participants.

Women in the ACS group were evaluated during hospitalization (first week after the acute event). Patients were identified as eligible by the attending cardiologist (according to the 'Third Universal Definition of Myocardial Infarction – Expert Consensus Document' by the European Society of Cardiology)<sup>24</sup> and were assessed for socio-demographic, behavioral, clinical, psychosocial variables and cardiovascular risk factors. Clinical variables associated with the ACS were obtained from patients' medical records and are shown in Table 1. Cardiac patients were excluded

if they were unable to fill self-evaluation questionnaires or had cognitive impairment (a score below or equal to 24 in the Mini-Mental State Examination).<sup>25</sup> Exclusion criteria for female controls included cardiovascular disease, either documented in clinical records or self-reported, and cognitive impairment (a score below or equal to 24 in the Mini-Mental State Examination).<sup>25</sup> Characteristics of the control group regarding socio-demographic, behavioral, psychosocial variables and cardiovascular risk factors are also shown in Table 1.

### Instruments

The Hospital Anxiety and Depression Scale (HADS) is a self-evaluation questionnaire which comprises two subscales, one measuring depression (HADS-D) and the other measuring anxiety (HADS-A).<sup>26,27</sup> The HADS is a present-state instrument, that is, it emphasizes on the condition within the last week. The HADS has been validated for the Portuguese population in different patient groups (including patients with coronary heart disease)<sup>28</sup> and is also recommended for use in community settings and primary health care. The HADS consists of two subscales, one measuring anxiety and the other depressive symptoms which are scored separately. Each subscale consists of seven items, answered by the patient on a 4 - point scale (0 to 3) so that the scores can vary from 0 - 21. According to the HADS manual, a HADS cutoff score of greater than 7 in any of the subscales indicates the presence of symptoms, i.e. HAD-D  $\geq$  8 indicates depressive symptoms<sup>27</sup> and this cutoff was also used in the present study. Also, the HADS has been considered more consistent in evaluating depression in ACS patients for containing less somatic symptoms that could be more readily influenced by health status.<sup>29</sup>

A Portuguese version of the type-D scale-14 (DS-14) has been validated for the Portuguese population and was used in this study to measure type-D personality.<sup>30</sup> The DS-14 consists of 14 items, 7 assessing negative affectivity (NA) and the other 7 assessing social inhibition (SI). Each item is rated on a five-point scale, ranging from 0 to 4. A score of at least 10 in both sub-scale identifies individuals as having type-D (or distressed) personality.<sup>17</sup> In this study we used a cut-off of 10 for both subscales which is considered to be the most reliable for use in clinical samples, including patients with cardiovascular disease and in the general population. According to Emons *et al*,<sup>31</sup> in a study using item response theory, all items had highest measurement precision around the cut-off measurements and were fairly comparable across the general population and clinical populations.

### Data analysis

In this study, we started by comparing a set of cardiovascular risk factors and psychosocial measures between the group of first ACS episode female patients and the group of age-matched female controls. Next, we sought to identify predictors of ACS among the patients group to examine whether any psychosocial measure could contribute independently to a higher risk of ACS.

Table 1 - Baseline characteristics of participants

Variables	Control group (n = 43)	ACS group (n = 34)	p
<b>Demographic characteristics</b>			
Age (M ± SD)	64.3 ± 8.2	65.7 ± 9.5	0.49
Education (M ± SD)	8.2 ± 3.9	5.4 ± 4.1	<b>0.003</b>
Living alone (%)	16.3	14.7	0.850
<b>Lifestyle characteristics</b>			
Smoking (%)	23.3	14.7	0.347
Alcohol consumption (%)	23.3	38.2	0.154
Exercise (%)	58.1	26.5	<b>0.005</b>
<b>Clinical characteristics</b>			
BMI (M ± SD)	25.7 (4.4)	26.8 (4.6)	0.278
Hypertension (%)	25.6	76.5	<b>&lt; 0.001</b>
Diabetes (%)	4.7	20.6	<b>0.031</b>
Dyslipidemia (%)	34.9	70.6	<b>0.002</b>
<b>ACS characteristics</b>			
Diagnosis			
NSTEMI / unstable angina	NA	64.7	
STEMI	NA		
Anterior		5.9	
Inferior		14.7	
Lateral		8.8	
Undetermined		5.9	
LVEF			
> 55%	NA	76.4	
40% - 55%		11.8	
30% - 40%		11.8	
CABG (%)	NA	8.8	
Troponin (M ± SD)	NA	20.5 ± 26.1	
Systolic BP (M ± SD)	NA	141 ± 27.5	
Diastolic BP (M ± SD)	NA	79.8 ± 17.2	

M ± SD: Mean ± Standard deviation; BMI: Body Mass Index; ACS: Acute coronary syndrome; NSTEMI: Non-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; LVEF: Left ventricular ejection fraction; CABG: Coronary artery bypass graft; BP: Blood pressure; NA: Non applicable

Finally, we assessed whether a positive status for type D personality would be associated with worse psychological adjustment, in terms of anxiety and depression symptoms, and whether this link would be more evident among patients.

All analyses were carried out with the Statistical Package for the Social Sciences – SPSS (version 19). Exploratory analyses examined the normality of the distribution of data points for each group (patients/controls) with the Shapiro-Wilk test. No transformation was deemed necessary for the sampled data. Univariate analyses compared demographic, behavioral, clinical, and psychometric variables between the control group and the ACS group. Differences between proportions were examined with Chi-squared tests whereas mean comparisons were conducted with Student *t* tests. The homogeneity of variances was inspected through the Levene test, and the appropriate *t* values adjusted for the corrected degrees of freedom were considered in those instances of significantly uneven variances. A multiple

logistic regression analysis (backward LR method) was conducted to quantify the independent associations of previously identified correlates with cardiovascular disease. The assumption of non-collinearity in the logistic regression model was studied through an exploratory analysis of nonparametric Spearman's bivariate correlation coefficients, which were initially computed between the categorical predictors. Spearman's *r* ranged between -0.12 (use of antidepressants x hypertension) and 0.57 (type-D personality x anxiety), but most correlations lagged behind 0.30. Therefore, the data matrix did not require any transformation. Adjusted odds ratios (OR) with 95% confidence intervals were included in the model summary. A series of 2 group (ACS patients, controls) by personality status (type-D, non-type-D) ANOVAs were conducted on anxiety and depression scores (HADS-A; HADS-D). The assumption of homogeneity of variances for the ANOVAs was again inspected with the Levene test. No

violation was detected for both dependent variables (anxiety scores: Levene's  $F = 0.248$ ;  $p = 0.621$ , for the patients vs controls comparison within the non-type-D participants; Levene's  $F = 0.002$ ;  $p = 0.964$ , for the patients vs controls comparison within the type-D participants; depression scores: Levene's  $F = 0.027$ ;  $p = 0.869$ , for the patients versus controls comparison within the non-type-D participants; Levene's  $F = 0.004$ ;  $p = 0.952$ , for the patients versus controls comparison within the type-D participants). Measures of effect size (Cohen's  $d$ , phi, odds ratio, and eta squared) were reported as required. A statistical significance level of  $p < 0.05$  was considered for all analyses.

## RESULTS

### Univariate analyses

Baseline characteristics were compared between control and ACS patients groups (see Table 1). Although groups were initially matched for age ( $64.3 \pm 8.2$  vs  $65.7 \pm 9.5$ ;  $t = -0.71$ ;  $p = 0.49$ ;  $d = 0.16$ ), controls had significantly more years of education ( $8.2 \pm 3.9$  vs  $5.4 \pm 4.1$ ;  $t = 3.13$ ;  $p < 0.05$ ;  $d = 0.71$ ). As to lifestyle characteristics and CVD risk factors, ACS patients had significantly lower levels of exercise ( $\chi^2 = 7.72$ ;  $p = 0.005$ ;  $\phi = -0.32$ ), and more hypertension ( $\chi^2 = 19.70$ ;  $p < 0.001$ ;  $\phi = 0.51$ ), diabetes ( $\chi^2 = 4.67$ ;  $p = 0.031$ ;  $\phi = 0.25$ ) and dyslipidemia ( $\chi^2 = 9.68$ ;  $p = 0.002$ ;  $\phi = 0.36$ ). No significant differences were found between groups for smoking ( $\chi^2 = 0.89$ ;  $p = 0.347$ ;  $\phi = -0.11$ ), alcohol consumption ( $\chi^2 = 2.03$ ;  $p = 0.154$ ;  $\phi = 0.16$ ), and BMI ( $t = -1.09$ ;  $p = 0.278$ ;  $d = -0.25$ ). The ACS group included 22 patients with a diagnosis of non-ST elevation myocardial infarction (NSTEMI)/ unstable angina and 12 patients with ST-elevation myocardial infarction (STEMI). From the total, 76.4% patients had a left ventricular ejection fraction (LVEF) in normal range and only 8.8% of patients were treated with coronary artery bypass graft surgery (CABG) (see Table 1). Considering psychosocial factors (Table 2), type-D personality

( $\chi^2 = 11.78$ ;  $p = 0.001$ ;  $\phi = 0.39$ ) and anxiety symptoms (HADS-A,  $\chi^2 = 27.12$ ;  $p < 0.001$ ;  $\phi = 0.59$ ) were significantly more prevalent among ACS patients, whereas the groups did not differ on prevalence of either depressive symptoms (HADS-D,  $\chi^2 = 1.93$ ;  $p = 0.165$ ;  $\phi = 0.16$ ) or psychiatric referrals ( $\chi^2 = 0.05$ ;  $p = 0.816$ ;  $\phi = -0.03$ ). Curiously, antidepressant medication was significantly more common among the control group ( $\chi^2 = 6.19$ ;  $p = 0.013$ ;  $\phi = 0.28$ ).

### Multiple logistic regression analysis

A multiple logistic regression analysis (Nagelkerke  $R^2 = 0.576$ ) for the independent correlates of female ACS (Table 3) revealed that hypertension ( $p = 0.014$ ; OR = 5.103), dyslipidemia ( $p = 0.049$ ; OR = 3.768), more anxiety (HADS-A) symptoms ( $p = 0.047$ ; OR = 4.315), type-D personality ( $p = 0.045$ ; OR = 4.605), and less antidepressant use ( $p = 0.008$ ; OR = 0.045) were all independently associated with ACS.

### Type-D personality impact on anxiety and depression symptoms

A series of two group (ACS patients, controls) by two personality status (type-D, non-type-D) ANOVAs were conducted on HADS-A and HADS-D scores (Fig. 1). Overall, significant main effects on HADS-A were found for group [ $F(1.73) = 8.01$ ;  $p < 0.05$ ;  $\eta^2 = 0.10$ ] and personality status [ $F(1.73) = 11.90$ ;  $p < 0.001$ ;  $\eta^2 = 0.14$ ]. Specifically, ACS patients ( $M = 10.52$ ;  $SE = 0.69$ ) had significantly higher anxiety scores than controls ( $M = 5.42$ ;  $SE = 0.64$ ). Similarly, type-D participants ( $M = 11.10$ ;  $SE = 0.80$ ) scored significantly higher than non-type-D counterparts ( $M = 6.21$ ;  $SE = 0.61$ ). Moreover, anxiety symptoms varied within each group, depending on the participants' personality status [ $F(1.73) = 3.47$ ;  $p = 0.07$ ;  $\eta^2 = 0.05$ ]. Accordingly, type-D participants ( $M = 10.33$ ,  $SE = 1.57$ ) had significantly higher scores ( $t = -3.32$ ,  $p < 0.05$ ) than non-type D participants ( $M = 4.62$ ;  $SE = 0.63$ ) within the control group, whereas both

Table 2 - Univariate analyses of participants' psychometric outcome

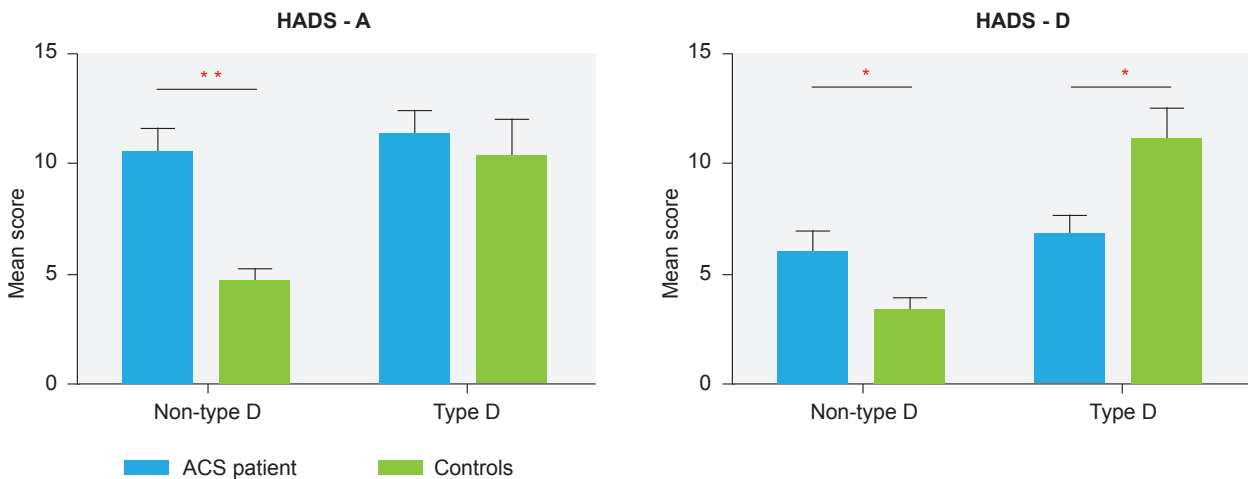
Variables	Control group (n = 43)	ACS group (n = 34)	p
DS – 14 Type D (NA $\geq 10$ and SI $\geq 10$ ) (n, %)	6 (14.0)	17 (50)	<b>0.001</b>
HADS – A $\geq 8$ (n, %)	11 (25.6)	29 (85.3)	<b>&lt; 0.001</b>
HADS – D $\geq 8$ (n, %)	8 (18.6)	11 (32.4)	0.165
Current antidepressant medication (n, %)	12 (27.9)	2 (5.9)	<b>0.013</b>
Psychiatric history (n, %)	15 (38.9)	11 (32.4)	0.816

HADS–A: Hospital Anxiety and Depression Scale – Anxiety; HADS–D: Hospital Anxiety and Depression Scale – Depression; DS-14: Type-D Scale; NA: Negative affectivity; SI: Social inhibition; ACS: Acute coronary syndrome

Table 3 - Multiple logistic regression analysis model summary for the independent correlates of female ACS\*

Correlates	B	S.E.	Wald 2	df	Odds ratio	95% C.I.	p
Hypertension	1.630	0.660	6.093	1	5.103	1.399 18.612	<b>0.014</b>
Dyslipidemia	1.327	0.672	3.892	1	3.768	1.009 14.079	<b>0.049</b>
HADS-A	1.462	0.735	3.962	1	4.315	1.023 18.205	<b>0.047</b>
DS–14 Type D	1.527	0.761	4.027	1	4.605	1.036 20.465	<b>0.045</b>
Current antidepressant medication	-3.111	1.164	7.147	1	0.045	0.005 0.436	<b>0.008</b>

\* Backward Likelihood Ratio procedure; ACS cases coded as 1. HADS–A: Hospital Anxiety and Depression Scale – Anxiety; HADS–D: Hospital Anxiety and Depression Scale – Depression; ACS: Acute coronary syndrome



**Figure 1** - Mean HADS-A and HADS-D scores stratified by personality status (non-type D vs type D) and group (control vs ACS patients) HADS-A: Hospital Anxiety and Depression Scale – Anxiety; HADS-D: Hospital Anxiety and Depression Scale – Depression; ACS: Acute coronary syndrome. Paired comparisons revealed that among the non-type-D participants, ACS patients displayed significantly more symptoms of anxiety ( $t = -4.49$ ;  $p < 0.001$ ) and depression ( $t = -2.24$ ;  $p < 0.05$ ) than controls. Interestingly, this effect inverted for type-D participants and HADS-D scores ( $t = 3.10$ ;  $p < 0.05$ ). Error bars were plotted using the standard error of the mean (SE). \*  $p < 0.05$ , \*\*  $p < 0.001$ .

non-type-D ( $M = 9.67$ ;  $SE = 0.98$ ) and type-D ( $M = 11.37$ ;  $SE = 0.94$ ) ACS patients had similar scores ( $t = -1.26$ ;  $p = 0.22$ ; n.s.). Correspondingly, a significant main effect of personality status [ $F(1.73) = 20.85$ ;  $p < 0.001$ ;  $\eta^2 = 0.22$ ] was also found on HADS-D scores, with type-D participants ( $M = 7.84$ ;  $SE = 0.72$ ) reporting significantly more depressive symptoms than non-type-D ( $M = 4.00$ ;  $SE = 0.52$ ). Furthermore, a significant group  $\times$  personality status interaction effect on the HADS-D scores was also found [ $F(1.73) = 11.82$ ;  $p < 0.05$ ;  $\eta^2 = 0.14$ ]. Similarly to HADS-A, depressive symptoms were significantly more prevalent in type-D ( $M = 11.00$ ;  $SE = 1.18$ ) than in non-type-D participants ( $M = 3.24$ ;  $SE = 0.61$ ) within the control group ( $t = -4.88$ ;  $p < 0.001$ ), whereas no difference was found ( $t = -0.97$ ;  $p = 0.34$ ; n.s.) between non-type-D ( $M = 5.63$ ;  $SE = 0.87$ ) and type-D ( $M = 6.72$ ;  $SE = 0.71$ ) ACS patients.

## DISCUSSION

We compared ACS female patients with age-matched female controls on cardiovascular and psychosocial factors to determine whether any psychosocial measure would be independently associated with ACS, and whether type-D personality, a stable personality trait, would be associated with more anxiety and depression symptoms among patients. Not surprisingly, we found higher prevalence of hypertension, diabetes and dyslipidemia among patients compared to controls. We also found a higher prevalence of type-D personality and anxiety symptoms in patients even though no differences were found regarding the prevalence of depressive symptoms. In fact, antidepressant medication was more commonly used by controls. High anxiety scores in patients might reflect an adaptive psychological response to the ACS, which is a major life-threatening event, and not necessarily a true anxiety disorder. In addition, we identified type-D personality as an independent psychosocial predictor of risk for ACS in females. Furthermore, our findings also indicate that type-D personality is associated with more

depressive and anxious symptomatology, albeit revealing a distinct expression by group.

Low education generally inflates the prevalence of traditional CVD risk factors such as hypertension and diabetes.<sup>32</sup> Therefore, we cannot exclude the possibility that patients' educational level might have accentuated their prevalence. However, smoking and alcohol consumption habits have also been associated with a low education level, yet no differences were detected for these risk factors. Regarding psychosocial measures, the prevalence of type-D personality was unusually high among patients, whereas controls yielded a prevalence rate which was lower than other community estimates.<sup>17,18,21</sup> Similarly, the prevalence rate of clinically relevant anxiety symptoms was significantly higher among patients who might reflect an adaptive response to the ACS. However, evidence indicates that anxiety worsens the prognosis of cardiac patients by increasing the risk for recurrent cardiovascular events and thereby the risk of cardiac mortality.<sup>13,14</sup> Further, anxiety is also an independent risk factor for CVD in community samples,<sup>14,15</sup> which makes 26% of control participants a disturbing estimate of clinical anxiety. Unexpectedly, no significant group difference was found in the prevalence rate of depressive symptoms. This null finding may result from a small sample size combined with a high prevalence of depressive symptoms among controls, as suggested by their frequency of antidepressants use. Still, 32% of patients had clinical symptoms of depression. A similar (31% - 45%) rate of patients presenting clinical symptoms following an ACS has been reported elsewhere.<sup>33</sup> In addition, depression increases the risk for cardiac morbidity and mortality in the general population<sup>11,12</sup> which makes the estimate of clinical symptoms among female controls also a concern. Nonetheless, antidepressants use and psychiatric referrals were significantly less common among patients. This finding may reflect the general assumption that depression remains largely under-recognized and under-treated in

cardiac patients, although safe and effective antidepressant treatments are available.<sup>33</sup>

In this study, several independent predictors of ACS were identified. Among the traditional CVD risk factors assessed, dyslipidemia and hypertension increased the likelihood for an ACS in a 3- and 5-fold risk, respectively. Such independent contributions to ACS risk are well documented in longitudinal studies.<sup>34,35</sup> We also found that the presence of type D personality and less frequent antidepressant use were all independent predictors of ACS. Whereas the latter may reflect a systematic influence in this particular population (i.e., reluctance by clinicians in prescribing antidepressants), the 4-fold increase in risk for ACS associated with type-D personality is worth highlighting. Although beyond the scope of this study, putative mechanisms mediated by anxiety symptoms and/or distressed personality may implicate a combination of heightened autonomic reactivity, changes in platelet function, and endothelial dysfunction subsequent to periods of stress exposure.<sup>7,36</sup> Nevertheless, the identification of clinical predictors can help outline a high risk profile which may guide prevention strategies in women and lead to an optimization of resources. Accordingly, type-D personality coupled with hypertension and dyslipidemia, delineated such a profile.

Contrary to what is commonly believed,<sup>37,38</sup> type-D personality was not associated with increased anxiety and depression symptoms among patients. This finding is particularly striking given that type-D personality is usually associated with higher levels of stress, mental distress, and increased physical symptoms in cardiac patients.<sup>39</sup> However, type-D personality was indeed associated with increased anxiety and depression symptoms among the controls. This interesting finding can have several interpretations. First, the fact that both patients and controls scoring positive for type-D personality were indistinct regarding anxiety symptoms suggests that type-D personality could have acted as a 'buffer' through a mechanism of stress cognitive appraisal<sup>40</sup> following the cardiac event (i.e., acute stressor). Second, type-D personality patients had significantly less depressive symptoms than their control counterparts. It could be hypothesized that type-D personality participants resort to negative affectivity as an emotional coping strategy, which becomes less responsive once a life-threatening event occurs. In fact, other studies have also found that negative affectivity was unrelated to depressive symptoms following an AMI,<sup>41</sup> and that depression was unrelated to CVD severity in type-D patients.<sup>42</sup> In other words, our data overall suggest that type-D works as a risk factor for cardiac events by amplifying the expression of negative affect, and that this influence becomes diminished once the disease is established.

Our study has some limitations that we acknowledge. First, our sample size hinders generalization of findings and could have limited power to unmask hidden effects (see above). Second, although type-D personality was

associated with both anxiety and depressive symptoms differently by group, this study employed a cross-sectional design thus making the valuation of type-D personality influences over time speculative, at best. However, to our knowledge, this study is pioneer in examining these associations with a female-specific focus. Women are still under-represented in clinical cardiovascular research although evidence of clear-cut gender differences in biomedical and psychosocial risk factors and medical outcomes urges further research in women.

The evaluation of psychosocial risk factors in women with CVD would contribute to better risk stratification and help the clinician to provide adequate intervention if required. Studies examining the benefits of psychological interventions in cardiac patients have shown varying results, some pointing out no clear benefits whilst others have reported significant reductions in mortality.<sup>43</sup> The Stockholm's Women's Intervention Trial for Coronary Artery Disease (SWITCHD) indicated that psychosocial interventions could produce an almost 3-fold higher protective effect on mortality compared to standard medical care.<sup>44</sup> Those interventions aimed to control behavioral risk factors, attenuate negative emotions, improve coping skills, reduce stress, and improve social support.<sup>44</sup> It is generally accepted that psychosocial interventions in patients with CVD illness should focus on the training and practice of social and coping skills so that patients can better handle stressful situations and experience less negative affect.<sup>45</sup> However, to our knowledge, no studies have evaluated the cardiovascular impact of those interventions among female type-D personality patients.

## CONCLUSIONS

Our findings indicate that female ACS patients reveal a disproportionate prevalence of type-D personality, fact that merits clinical attention since type D personality is known to facilitate additive effects of hypertension and dyslipidemia in terms of worse cardiac prognosis. However, in this study, the levels of anxiety and depression reported by patients following an acute cardiac event were apparently unrelated to type-D personality, a pattern that clearly contrasted with that of controls. Future research should examine how psychosocial factors cluster in women and which putative mechanisms allow them to interact with acute cardiovascular events. Moreover, it is priceless to determine whether interventions aimed at type-D personality are beneficial in terms of mortality decrease and quality of life improvements. Ultimately, this will translate into more effective female-specific prevention strategies and better patient outcomes.

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## PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

## DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

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## CONFLICTS OF INTEREST

All authors report no conflict of interest.

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