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The role of alexithymia in predicting incident depression in patients at first acute coronary syndrome

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Abstract

Objective: Alexithymia has been considered both to predispose to depression and to worsen cardiac prognosis after an acute coronary syndrome. Nonetheless, no studies have evaluated its role as a risk factor for incident depression, in patients with acute coronary syndrome.
Methods: In 251 consecutive patients, the presence of a first-ever depressive episode was evaluated with the Primary Care Evaluation of Mental Disorders at baseline and 1, 2, 4, 6, 9, 12 and 24 months after their first acute coronary syndrome. At baseline, patients completed the Toronto Alexithymia Scale (TAS-20) and the Hospital Anxiety and Depression Scale.
Results: Out of 251 subjects (80.9% males), a first-ever depressive episode was diagnosed in 66 patients. Depressed and never-depressed patients differed in female gender, living status, alexithymic scores at TAS-20 and depressive symptoms. Nonetheless, nor the TAS-20 factors nor its total score were predictive of developing a depressive episode in a Cox regression. Moreover, baseline differences in TAS-20 scores between the two groups, disappeared after controlling for anhedonic symptoms.
Conclusion: Our results do not support the hypothesis that alexithymia at TAS-20 is a risk factor for incident depression after acute coronary syndrome.

1. Introduction

Alexithymia is a multidimensional construct characterized by an impoverished fantasy life, difficulty in expressing or naming feelings, difficulty distinguishing between bodily sensations and feelings and a preoccupation with external events [1]. The TAS-20 [2,3] is the most widely used and studied self-report measure of alexithymia. Factor analysis has supported a three-factor solution for this scale: (1) difficulty identifying feelings (DIF), (2) difficulty communicating and describing feelings (DDF), and (3) external-oriented thinking (EOT). Items representing impoverished fantasy or reduced daydreaming were dropped from the TAS-20 based on the factor analysis.

Alexithymia, reflecting a disordered affect regulation, is thought to increase vulnerability to several medical disorders, such as rheumatoid arthritis, essential hypertension, cardiac disease, stroke, peptic ulcer, inflammatory bowel disease, breast cancer, diabetes and kidney failure [4].

Moreover, high levels of alexithymia [5,6] or high rates of alexithymic subjects (21–32%) [7–9] were found in patients with coronary artery disease, suggesting that alexithymia could be a risk factor for it [10–12].

Alexithymia is also supposed to be a risk factor for the development of mental disorders, such as major depression [1,13,14], panic disorder, eating disorders and substance use disorders [15,16].

The association between depression and acute coronary syndrome is well-established [17] and depression is observed in 19.8% of patients who survive acute myocardial infarction [18].

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Depression in patients with acute coronary syndrome is associated with a worse cardiac outcome [19] due to an increase recurrence of cardiac events and mortality [20]. Moreover, a specific type of depression [21], characterized by higher anhedonia levels, has been supposed to be specifically related to cardiac outcome [22,23]. Risk factors for the development of depression after acute coronary syndrome have been also identified: younger age [24]; female gender [25] low level of education [26]; low socio-economic status [27]; having no close friend [28]; being unemployed and living alone [29]; type D personality [30]; psychological vulnerabilities (i.e. exhaustion, fatigue, interpersonal difficulties, cognitive distortions) [31–33]; the presence of depressive symptoms in the few days after an acute coronary syndrome [34,35]; and the severity of the acute coronary syndrome [24,36,37].

To our knowledge, no study investigated in patients with acute coronary syndrome whether alexithymia predicted the development of major depression. Previous studies observed that alexithymia was significantly related with anxiety and depression in acute coronary syndrome patients [9,11,38] and one study suggested that alexithymia is a consequence of acute myocardial infarction [38]. Furthermore, all the studies investigating alexithymia in coronary artery disease enrolled patients with previous episodes of coronary disease and most of these studies found an association between TAS-20 scores and pervious myocardial infarction or angina episodes [6–8,38].

These findings questioned whether the TAS-20 could measure negative affects associated with a general distress syndrome [15] or with a depressive episode [39] induced by recurrent episodes of coronary disease rather than alexithymia itself.

Therefore, the aim of this study is to evaluate whether alexithymia predicted the development of depressive episodes in never depressed patients at their first acute coronary syndrome.

2. Materials and methods

2.1. Sample

The study sample was selected among patients who were consecutively admitted to an Italian Coronary Intensive Care Unit from January 2009 to March 2012, for an acute coronary syndrome.

The local ethic committee has approved the study protocol, all the participants gave their informed consent after the study was fully explained and the study has been conducted according the Helsinki Declaration.

Patients were included in the study if at the time of enrolment: (1) their age was over 18 years; (2) they were native Italian speaker or with a proficiency in Italian; (3) they had no previous or current major depressive episode according DSM-IV [40]; (4) they had no substance abuse or dependence; (5) they did not show cognitive impairment as demonstrated by a Mini Mental State Examination (MMSE) [41] lower than 25; and (6) they did not take any psychotropic medication. (7) They presented for the first time with symptoms suggestive of an acute coronary syndrome and in whom an ST-segment elevation myocardial infarction (STEMI), a non–ST-segment elevation myocardial infarction (NSTEMI), or unstable angina had been diagnosed [24,43]. The working diagnosis of NSTE-acute coronary syndrome was a rule-out diagnosis based on the ECG, i.e. lack of persistent ST elevation. Biomarkers (troponins) further distinguished NSTEMI and unstable angina [42].

2.2. Assessment

All patients underwent the following evaluations at baseline: (1) a brief socio-demographic interview; (2) the Primary Care Evaluation of Mental Disorder (PRIME-MD) [44] to diagnose current or previous depressive episodes; (3) the Hospital Anxiety and Depression Scale (HADS) [45] that generates two subscale scores: the anxiety score (HADS-A) and the depression score (HADS-D); and (4) the Toronto Alexithymia Scale, 20 items (TAS-20) [2,3]. The TAS-20 generated four scores: difficulty identifying feelings (DIF) score, difficulty describing, communicating and expressing feelings to others (DDF) score, externally oriented thinking (EOT) score and TAS-20 total scores. A total score higher than 60 has been proposed to define someone as alexithymic. In this sample, the internal consistency for the TAS total score was $\alpha = .77$; (5) they were assigned a GRACE score which assesses mortality risk after acute coronary events [46]. The Global Registry of Acute Coronary Events (GRACE) score [47] is based on a risk model of 6 months mortality risk from the time of hospital discharge; it considers age, history of MI, past or current congestive heart failure (CHF), heart rate, systolic blood pressure, serum creatinine, elevated cardiac enzymes, ST-segment depression on ECG at admission, and no in hospital percutaneous intervention (PCI). All the information concerning the abovementioned parameters was obtained from chart review at baseline. The GRACE score ranges between 1 and 263 points. A score of 80 predicts a 1% mortality rate at six months, 100 predicts a 2% mortality rate, and >210 predicts a >50% mortality rate.

After the inclusion in the study, patients were re-evaluated one, two, four, six, nine, twelve and twenty-four months later with the PRIME-MD followed by a psychiatric interview to confirm a diagnosis a depressive episode.

2.3. Treatment

Concerning treatment of depression, patients with depressive symptoms were referred to a psychiatrist, and properly treated.

2.4. Statistical analyses

After computing the rates of patients classified as depressed and never-depressed over the course of follow-up, the baseline differences among groups were evaluated using

Fisher's exact test for categorical variables (i.e., gender, educational, family and occupational status) and t-test with for continuous variables (i.e. age, GRACE score, HADS and TAS-20 scores).

Analysis of covariance (ANCOVA) was used to evaluate whether, at baseline, the difference in TAS-20 scores among groups remained after controlling for the effect of depressive symptoms.

Previous results in literature [48,49] confirm the high correlation found between HADS-A and HADS-D ($r = .777$, $p < 0.001$). In order to avoid collinearity between the covariates at the ANCOVA, we performed an exploratory factor analysis of HADS. It identified two main factors: a first factor named negative affectivity (HADS-NA) where loaded mainly the items exploring low mood and worries (items 1, 3, 5, 6, 8, 10, 11 and 13) and a second factor named loss of pleasure or interest (HADS-LP) (items 2, 4, 7, 9, 12 and 14). Doing so, no more collinearity emerged between the two predictors (i.e. Tolerance > .02; VIF < 10; $r = .158$; $p = 0.01$; lower % of variance explained by the same small eigenvalue). Considering previous results [22,23,50] that suggested that low positive affectivity (i.e. anhedonic symptoms) is a core feature of depression in cardiac populations, we used the score of HADS-LP as a covariate in ANCOVA.

The cumulative incidence of depressive episode has been calculated over the follow-up as one minus the Kaplan–Meier survival probability.

A proportional hazard model (Cox regression, enter method) was used to evaluate which socio-demographic and clinical variables at baseline predicted the development of a depressive disorder during the follow-up period. We collapsed the family status in living alone that remained significant between the two groups, whereas dividing the sample in employed and unemployed/retired the differences were not significant anymore. Therefore, we entered the presence of a depressive episode as the state variables and its onset as time variable, whereas gender, living alone and the TAS-20 have been entered as independent variables.

Since alexithymia is not a unitary construct we performed separate regressions for each sub-score (i.e. DDF, DIF and EOT) and for the total score.

We carried out all the analysis using SPSS software (version 21.0, IBM SPSS Statistics).

3. Results

3.1. Patient characteristics

Three-hundred-and-ninety-seven patients met the inclusion criteria, and among them, 377 agreed to participate in the study. During the follow-up period 111 patients dropped (25 moved outside the study area and 21 continued the rehabilitation treatment in a different hospital after the enrolment, 65 refused further psychiatric evaluations, 15 passed away). Therefore, the study sample included 251 subjects (female n = 48, 19.1%), with a mean age of 61.3 ± 10.9 years (range 32–87 years).

3.2. Depressive disorder

Throughout the follow-up period, a depressive disorder was diagnosed in 66 patients (26.3%), of which 26 with major depression and 40 with minor depression, whereas 185 (73.7%) did not show any depressive disorder during the 2-years of follow-up. Onset of the depressive episode during the follow-up evaluation is shown in Fig. 1.

3.3. Socio-demographic characteristics

Female gender, being housewife and widowed were more frequent in the depressed group (Table 1).

3.4. Alexithymia

At baseline, the TAS-20 scores, except for DDF and EOT, were higher in depressed than in non-depressed patients with a small medium effect size (DIF: $d = 0.47$; TAS total score: $d = 0.33$). Moreover, based on the odd ratio of the chi-square test, the odds of patients with a new depressive episode were 3 times higher if they were alexithymic than if they were not ($\chi^2(1) = 8.7$; $p = 0.006$; OR = 2.97).

Nonetheless, among groups, the differences in TAS-20 scores disappeared after controlling for the effect HADS-LP scores (ANCOVA, DIF: $F = 4.25$; $df = 1248$; $p = 0.5$; partial $\eta^2 = .008$; TAS-20 total score: $F = 2.00$; $df = 1248$; $p = 0.16$; partial $\eta^2 = .016$).

3.5. Predictors of development of a depressive disorder

At the Cox regression any of the TAS-20 factors was a significant predictor of the onset of depression (Block 1: Female Gender OR = 1.21; 95%CI = 0.72–2.05; $\chi^2 = 0.52$; $p = 0.47$; Block 2: Female Gender OR = 1.22; 95%CI = 0.72–2.07; $\chi^2 = 0.53$; $p = 0.47$; Living Alone OR = 0.97; 95%CI = 0.56–1.68; $\chi^2 = 0.01$; $p = 0.93$; Block 3: TAS scores, in the four Cox regressions respectively, DIF OR = 1.01; 95%CI = 0.96–1.05; $\chi^2 = 0.09$; $p = 0.76$; DDF OR = 1.05; 95%CI = 0.99–1.12; $\chi^2 = 2.80$; $p = 0.09$; EOT OR = 1.01; 95%CI = 0.95–1.06; $\chi^2 = 0.06$; $p = 0.80$; TAS-20 total score OR = 1.01; 95%CI = 0.99–1.03; $\chi^2 = 0.73$; $p = 0.39$).

4. Discussion

The present study aimed to evaluate the role of alexithymia in predicting the first depressive episode (incident depression) in never-depressed patients after their first acute coronary syndrome.

All the previous studies evaluated alexithymia in patients with recurrent episodes of coronary artery disease and in this population alexithymia has been associated with previous myocardial infarction or angina episodes [6–8,38]. Moreover, in these patients alexithymia has also been related with

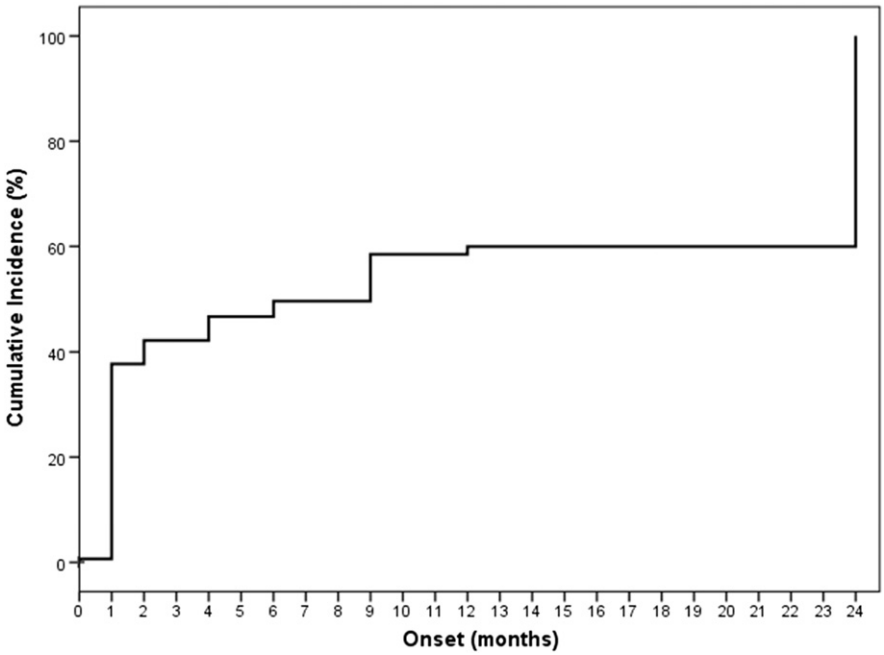

Fig. 1. Kaplan–Meier curve of the cumulative incidence, calculated as one minus survival, of depressive episodes (n = 66) over the follow-up period (2 years).

comorbid depression [9,11,38]. In contrast, in the present study alexithymia could not be associated at baseline with chronic coronary artery disease or with comorbid depression because only patients at their first acute coronary syndrome and without previous or current depressive episodes were enrolled.

In this study, patients who developed a depressive episode showed few days after their first acute coronary syndrome higher levels of DIF than subjects who maintained a non-depressed condition during the following year. Further, in those patients who developed depressive episode the rate of alexithymia at baseline was higher (24.2%) than in those who did not (9.7%), resulting in a three-fold increase in the risk of developing depression. Therefore, the TAS-20 scores assessed few days after an acute coronary syndrome and before the development of a depressive episode seem to increases the risk of depression, as suggested for patients without coronary artery disease [14,51–55].

Nevertheless, in the Cox regression analysis nor the TAS-20 total score at baseline nor the single factors predicted the development of a depressive episode.

There are at least two possible explanations for this finding.

Firstly, alexithymia may be a temporary response to a stressful condition, such as an acute coronary syndrome; in this view "secondary alexithymia" can represent a defense or a strategy to cope with distress (emotional pain, aversive memories and physiological arousal) associated with a life-threatening situation as previously hypothesized [38].

In the second hypothesis, the relationship between alexithymia and depression may represent an artifact of the method and measures used [63], since, particularly the TAS-20 dimensions DIF and DDF are associated with different measures of negative affects [15,16,56–63]. Therefore, individuals with negative emotional states (i.e. anxiety and depression) might score higher on these TAS-20 dimensions. This hypothesis is supported by previous studies, which found that alexithymia was significantly related with anxiety and depression in patients with an acute coronary syndrome [9,11,38].

Specifically, in the present study, the baseline differences in the difficulty in identifying feelings between depressed and never-depressed, disappeared after controlling for anhedonic symptoms. This result confirm previous data in literature that suggest that this factor of TAS-20 measures mainly a secondary alexithymia related to anhedonic symptoms of depression [64], but not others that did not found an overlap between anhedonia and alexithymia in healthy subjects [65]. Nonetheless, even those features of alexithymia that should be less state-dependent (i.e. EOT) [64,66], and not related to the anhedonic dimension in our sample ($r = .066$; $p = 0.30$) were not predictive of the development of depression.

The results of the present study do not support the notion that high TAS-20 scores increase the risk for developing a depressive disorder after an acute coronary syndrome, as already suggested in patients without coronary artery disease [67,68]. Instead, our results uphold the explanation that the assessment of alexithymia with TAS-20 few days after an acute coronary syndrome probably captures negative emotions following a life-threatening event. The data of this study also confirm the observation of significant relationships between alexithymia, assessed with the TAS-20, and negative affects or psychological distress

Table 1
Socio-demographic characteristics of patients distinguished according to their depressive condition.

	Depression	No Depression		
	n. 66	n. 185		
Gender (male)	46 (69.7%)	157 (84.9%)	$F^+ = 7.2$	p = 0.01
Age (years)	62.6 ± 10.7	60.8 ± 10.9	F = 0.3	p = 0.26
Education			$F^+ = 1.3$	p = 0.73
Primary school	13 (19.7%)	31 (16.8%)		
Lower secondary school	21 (31.8%)	73 (39.5%)		
Higher secondary school	27 (40.9%)	67 (36.2%)		
University	5 (7.6%)	14 (7.6%)		
Family status			$F^+ = 9.9$	p = 0.02
Never married	7 (10.6%)	22 (11.9%)		
Married	42 (63.6%)	142 (76.8%)		
Separated/divorced	7 (10.6%)	13 (7.0%)		
Widowed	10 (15.2%)	8 (4.3%)		
Living status (alone)	18 (27.3%)	24 (13.0%)	$F^+ = 7.1$	p = 0.01
Occupation			$F^+ = 9.2$	p = 0.03
Unemployed	2 (3.0%)	3 (1.6%)		
Retired	33 (50.0%)	96 (51.9%)		
Housewife	7 (10.6%)	4 (2.2%)		
Employed	24 (22.6%)	82 (44.3%)		
GRACE score	130.7 ± 29.0	131.0 ± 29.1	F = 0.07	p = 0.93
HADS scores at baseline				
Anxiety	9.27 ± 4.5	8.4 ± 5.5	F = 20.7	p = 0.22
Depression	8.33 ± 4.1	6.0 ± 4.1	F = 0.73	p < 0.001
TAS-20 scores at baseline				
DIF	17.1 ± 6.1	14.2 ± 5.5	F = 0.55	p = 0.02
DDF	13.5 ± 4.2	12.8 ± 4.2	F = 0.01	p = 0.19
EOT	21.4 ± 4.2	21.0 ± 4.4	F = 0.69	p = 0.55
Total	52.1 ± 12.1	48.1 ± 10.9	F = 0.59	p = 0.02
Total > 60	16 (24.2%)	18 (9.7%)	$F^+ = 8.7$	p = 0.006

HADS (Hospital Anxiety and Depression Scale): anxiety and depression subscales.
TAS-20 (Toronto Alexithymia Scale, 20 items): DIF, difficulty identifying feelings; DDF, difficulty describing feelings, EOT, externally-oriented thinking.
F = one-way ANOVA; F^+ = Fisher's exact test.

found in the general population [56,69]. Our data replicate the results of one of these studies [59] which found in the general population that the development of major depression was not predicted by TAS-20 score.

4.1. Limitations

Possible limitations of our study are the use of self-administered scale of alexithymia [70], where a structured interview is more stable and consistently related to negative affects. Therefore, the findings of the present study, based only on a self-reported measure of alexithymia, need to be confirmed by researches using on observer ratings (e.g., Toronto Structured Interview for alexithymia) [71] or objective performance-based tasks such as the Levels of Emotional Awareness Scale [72].

Moreover, we cannot say when the feeling of anxiety and worries as much as the feelings of lack of pleasure or interest observed few days after the cardiac event appeared, specifically if their appearance preceded or followed the occurrence of the acute coronary syndrome. Regardless they represent a psychological disposition or a psychological reaction to an acute coronary syndrome, they do not satisfied at the time of inclusion in the study the diagnostic criteria for a major depressive episode.

5. Conclusion

The present study supports the hypothesis that the TAS-20, the most widely used self-administered scale assessing alexithymia, is overly sensitive to a general distress syndrome, and therefore it is more likely to measure negative affects (distress, nervousness, fear, anger, guilt, sadness, scornfulness) rather than alexithymia itself. In this view, patients after the first acute coronary syndrome reported high levels of alexithymia, assessed with TAS-20, because they present a psychological distress rather than a personality characterized by disordered affect regulation.

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Conflict of Interest

None.

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