



## Correlation of positive psychological states with cortisol awakening response's flexibility and lower levels of hs-CRP in coronary artery patients

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### ARTICLE INFO

#### Article history:

Received: 16 February 2014;

Received in revised form:

22 February 2014;

Accepted: 1 March 2014;

#### Keywords

Coronary artery disease,

Depression,

C-reactive protein,

Cortisol,

Positive psychology.

### ABSTRACT

Previous studies emphasizing that psychological interventions and pharmacological medications may have a small effect on depressive symptoms in coronary artery patients, and no beneficial effects on reduction of inflammatory markers and mortality rates. Recently there is increasing interest in whether positive psychological states have predictive power over and above depressive symptoms for cardiovascular disease and all-cause mortality. The present study has intended to test and compare the correlation of plasma high sensitivity C-reactive protein and cortisol awakening response's flexibility with positive psychological states and depression in 54 coronary artery patients. The results of this study indicated that the correlation between high sensitivity C-reactive protein and psychological states only for life satisfaction and subscale of hope "pathways in regard to goals" are significant. Moreover the correlations of cortisol awakening response's flexibility with happiness, hope and depression were marginally significant. It is possible that directly building the positive psychological states may counteract negative symptoms and may also buffer against their negative biological outcomes.

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### Introduction

Converging evidence suggests that the increased mortality related to depressive symptoms in patients with coronary artery disease (CAD) may be induced by biological mechanisms that might link these two conditions to each other [1]. Abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis [2] and increased inflammation [3] are two of the most consistent findings in depression. The HPA abnormalities found in major depression (MD), extensively studied include increased secretion and reactivity of cortisol [4] elevated basal cerebrospinal fluid corticotropin-releasing hormone (CRH) levels [5] and increased size as well as activity of the pituitary and adrenal glands [6]. Most studies on morning salivary cortisol have also demonstrated an increased awakening response in depressed subjects [7] and in subjects with subclinical depressive symptoms [8].

Similarly, previous findings suggest that C-reactive protein (CRP) as the most studied inflammatory marker [9] should be positively associated with the incidence and severity of depression in patients with coronary artery disease [10]. CRP is synthesized in the liver as an integral part of acute phase response in association with inflammation, tissue necrosis and cell injury [11]. Plasma CRP levels would then reflect the severity of atherosclerosis and may be useful in predicting cardiovascular events and mortality in patients with coronary heart disease [12].

At the same time recent studies have been suggested that positive psychological states such as happiness, positive emotions and optimism are associated with healthy HPA axis functioning and reduced inflammation. For instance a number of

studies have shown that cortisol tends to be lower when people have greater positive affect [13]. Steptoe and Wardle (2005) found that greater happiness is associated with lower salivary cortisol both on working and nonworking days and persisted in a repeated assessment of the same individuals after 3 years [14]. Associations between lower cortisol and positive affect have also been reported in a community sample in the USA [15], and in a sample of Hong Kong Chinese [16]. Ryff et al. (2004) found that women with higher levels of positive well-being have lower levels of cortisol early in the day, and this level is maintained over the rest of the day [17].

Similarly, Brouwers et al. (2013) indicated that positive affect is associated with reduced inflammation in patients with heart failure [18]. Importantly, the relation of positive psychological states with physiological pathways occurs in addition to the effects of negative feelings and depression, suggesting that positive psychological states may have distinctive biological correlates that can benefit health [19].

While treatment of depression in CAD patients has not resulted in reduction of inflammation and mortality rates, since positive psychology is a new movement, comparative studies have not developed in this setting. The present study has intended to test and compare the correlation of plasma high sensitivity C-reactive protein (hs-CRP) and cortisol awakening response (CAR)'s flexibility with positive psychological states and depression in coronary artery patients.

### Materials and Methods

#### Procedures and Participants:

From CAD patients referring to the Iran Zamin cardiac rehabilitation center and Sina cardiovascular hospital in Isfahan

city, 313 patients who had received coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PCI) were called randomly and invited to the study. Inclusion criteria included being documented CAD patient and receiving CABG or PCI. Exclusion criteria were as follows: (a) medical condition limiting ability to participate in the study and (b) unwillingness to participate in all stages of study. Fifty four patients who had appropriate criteria participated in the study.

### Instruments and Data collection

#### Psychological measures:

##### Oxford Happiness Inventory

The Oxford Happiness Inventory is a 29-item multiple choice instrument. The highest score that a subject can get on the scale is 87, and the lowest score is zero. [20]

##### Beck Depression Inventory

The long form of Beck Depression Inventory (BDI-II) contains 21 items. The range of scores is between 0 and 63. This inventory is comprised of affective, cognitive and somatic subscales. [21]

##### Satisfaction With Life Scale (SWLS)

The SWLS is a short 5-item scale which measures global cognitive judgment of satisfaction with life. This scale designed by Diener and his colleagues (1985) [22].

##### Dispositional Hope Scale

This scale is consisted of 12 items: four are distracters, four tap agency for goals and four tap pathways thinking in regard to goals. Scores can range from a low of 8 to a high of 64 points [23].

### Biological markers in data collection:

#### hs-CRP

To assess CHD risk, CRP must be measured by high sensitivity methods (hs-CRP) that are capable of reliably measuring concentrations within the healthy reference interval [24]. Participants were instructed to fast and to avoid caffeine for 12 hours prior to blood sampling. Serum aliquots were frozen at  $-70^{\circ}\text{C}$  until the time of assay. The hs-CRP was measured with nephelometric assay for quantitative determination of low levels of C-reactive protein (Bionik Diagnostic system kit, Iran) with Mininephnephelometer (UK).

#### Cortisol Awakening Response

Participants were instructed to start sampling immediately at awakening (0), 15 and 45 min after awakening in the morning. Saliva sampling took place at home on two different days (workday and the day of rest). For retired participants or housewives the less busy days of the week was considered as a day of rest and the busiest day of the week was considered as working days. Cortisol was assayed with the enzyme-linked immunosorbent assay (ELISA) kits (DiaMetra, Italy) and Awareness analyzer (Awareness Technology, USA). Six cortisol parameters were computed for each participant on each assessment stage of the study. The area under the curve (AUC) with respect to ground ( $\text{CAR}_g$ ) and the area under the curve with respect to the increase ( $\text{CAR}_i$ ) [25] for workday and day of rest,

and difference between the workdays and day of rest CARs ( $\Delta\text{CAR}$ ) for  $\text{CAR}_g$  and  $\text{CAR}_i$  were calculated [26].

### Statistical Analysis

The correlations of psychological variables with plasma levels of hs-CRP and CARs were examined through Pearson Correlations. The data were analyzed using SPSS for Windows software (version 18.0).

### Results:

Demographic and medical characteristics of groups are

**Table 1. Demographic and medical characteristics of patients**

Characteristics	Values
Number of subjects	54
Male (%)	39 (72.2%)
Age( $\pm$ SD)	55.8 ( $\pm$ 8.4)
Maximum	76
Minimum	31
Married (%)	47 (87%)
Employment (%)	23 (42.6%)
Mean of education (years) ( $\pm$ SD)	10.5( $\pm$ 1.7)
Economic status (%):	
High	9.3
Good	13.1
Average	70.2
Weak	7.4
Time since diagnosis(year) ( $\pm$ SD)	3.7 ( $\pm$ 3.9)
Type of medical intervention (N / %):	
Balloon angioplasty	18 (33.3%)
Stents	7 (13%)
CABG	18 (33.3%)
Multiple interventions	11 (20.4%)
Comorbidities (N / %):	
Diabetes	11 (20.4%)
Hypertension	21 (38.9%)
Arthritis	14 (25.9%)
Back problems	7 (13%)
Others	5 (9.3%)

depicted in table 1.

### The correlations among the psychological variables and hs-CRP

We performed bivariate correlation test among psychological factors and hs-CRP levels in CAD patients. Results of this correlation test have come in table 2.

### Results for CARs

Results of the test for correlations among the psychological variables and cortisol parameters (CARs) are depicted in table 3. These results also reveal that CAR flexibility is a better indicator of psychological state than CAR magnitude.

**Table 2. Result of the test for correlations among the psychological variables and hs-CRP**

Variable	Statistical index	Happiness	Depression	Life satisfaction	Hope	Agency for goals	Pathways in regard to goals	Depression affective symptoms	Depression cognitive symptoms	Depression somatic symptoms
hs-CRP	r	-0.072	0.130	-0.323*	-0.259	-0.165	-0.302*	0.066	0.163	0.112
	sig	0.604	0.350	0.017	0.059	0.232	0.026	0.634	0.238	0.418

Note:\* significant at the level of  $p < 0.05$

**Table 3. Results of the test for correlation among the psychological variables and cortisol parameters (CARs)**

Variables	index	CAR <sub>g</sub> rest	CAR <sub>g</sub> work	CAR <sub>i</sub> rest	CAR <sub>i</sub> work	$\Delta$ CAR <sub>g</sub>	$\Delta$ CAR <sub>i</sub>
Happiness	r	-0.04	0.109	0.04	0.157	0.200	0.117
	p	0.39	0.22	0.39	0.13	<b>0.07</b>	0.20
Depression	r	-0.036	-0.170	0.027	-0.12	-0.211	-0.149
	p	0.40	0.11	0.42	0.19	<b>0.06</b>	0.14
Life satisfaction	r	0.214	0.187	-0.005	0.059	0.056	0.064
	p	0.06	0.09	0.49	0.34	0.34	0.32
Hope	r	0.109	0.210	0.099	0.147	0.195	0.045
	p	0.22	0.06	0.24	0.15	<b>0.07</b>	0.373

### Discussion:

The cardiac mortality relative risk in cardiac patients increased to 3.8 for those who were clinically depressed [27] and it has been suggested that abnormalities in the hypothalamic-pituitary-adrenal axis and inflammation are physiological missing links between coronary artery disease (CAD), depression and increased risk of mortality in this population. However, the field suffers from a lack of well-designed clinical interventions and treatment of depression in heart disease patients has not resulted in improved cardiac outcomes [28]. Recently there is increasing interest in whether positive psychological constructs have predictive power over and above depressive symptoms for cardiovascular disease (CVD) and all-cause mortality.

The results of this study show that the correlations among hs-CRP and psychological states only for life satisfaction and subscale of hope "pathways in regard to goals" are significant. Moreover the correlations among  $\Delta$ CAR<sub>g</sub> and positive psychological states, happiness and hope, were also marginally significant. These results are in line with an increasing body of evidence showing that positive affect is associated with superior cardiovascular outcomes. These beneficial effects including reduced risk for CHD [29], lower heart rate and blood pressure [30], lower salivary cortisol, lower cardiac mortality, superior cardiovascular outcomes( [13], fewer readmissions and increased survival following cardiac surgery [31].

The findings of present study are also consistent with previous studies confirming the beneficial effects of positive psychological states on the immune system and inflammatory markers [18, 30] and independency of these effects from negative affects including depressive symptoms [32]. The present study has shown that focusing on the enhancement of

positive psychological states may lead to more promising results than simply emphasizing on the treatment of depression. This is done while the previous studies emphasizing that psychological interventions and pharmacological medications with SSRIs may have no beneficial effects on cardiac outcomes or reduction of inflammatory markers, cardiac events and mortality rates [33].

Results of current study indicated that the hope as one of the most important positive psychological states was linked with reduced hs-CRP and increased CAR's flexibility. "The science of optimism and hope" has found that whether or not we have hope depends on two dimensions of optimism taken together. Finding permanent and universal causes of good events along with temporary and specific causes for misfortune is the art of hope; while acting contrary is the practice of despair [34]. In fact when someone has succeeded to boost his hope, this means that he has cultivated the optimism and all of its dimensions. However, the changes in both optimism and positive affect across time were associated with changes in immune responses [35].

As well as optimism has significantly linked to healthy autonomic function [36], reduced inflammation [37] lower incidence of CHD and cardiac mortality [38], fewer readmissions and increased survival following cardiac surgery [39]. Moreover Optimism and hope cause better resistance to depression [34].

These observations raise the hypothesis that the increase in positive psychological states, particularly hope, satisfaction with life and happiness may exert positive impacts on risk biomarkers in CAD patients. This study has suggestions for patients and therapists to test many and various techniques according to positive psychology for this vulnerable and important population with high rates of readmission and mortality. In fact it is

possible that directly building these positive states may counteract negative symptoms and may also buffer against their negative biological consequences.

#### Limitations:

There were some limitations in the current study that should be considered. There were patients who, following the CABG, were not willing to participate in the HTPs, which resulted in a small sample size. Potential researchers working with CAD patients should be aware of some challenges in applying group training for this specific population. The application of the same HTPs requires greater resources than other situations.

#### Source of Support:

This study was supported by Center of Excellence for Psychology of Spirituality and Happiness, The University of Isfahan, Isfahan, Iran.

#### Acknowledgment:

The authors would like to thank Iran Zamin cardiac rehabilitation Center and Sina cardiovascular hospital for their companion in this study. We are grateful to Farnaz Anari, Dr. Javad Alizadeh, Dr. Masoud Fesharaki, Saeedeh Hashemi and Shima Bateni, for their assistance in this study, and to Dr. Houshang Talebi and saeed hayati from the University of Isfahan and Dr. Mohammad Reza Merasi from the Isfahan University of Medical Sciences for their statistical consultation.

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