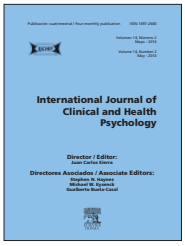
International Journal of Clinical and Health Psychology (2014) **14**, 111–119

International Journal of Clinical and Health Psychology

www.elsevier.es/ijchp



ORIGINAL ARTICLE

On the protective effect of resilience in patients with acute coronary syndrome

Antonio L. Arrebola-Moreno[a], Rocio Garcia-Retamero[b,c,*], Andrés Catena[b], Rafael Marfil-Álvarez[a], Rafael Melgares-Moreno[a], José A. Ramírez-Hernández[a]

[a] *Hospital Universitario Virgen de las Nieves, Spain*
[b] *Universidad de Granada, Spain*
[c] *Center for Adaptive Behavior and Cognition, Max Plank Institute for Human Development, Germany*

Received October 3, 2013; accepted February 3, 2014

KEYWORDS
Resilience;
Inflammation;
Acute myocardial infarction;
Acute coronary syndrome;
Cross-sectional study

Abstract Research on the contribution of positive personality traits to the progression of coronary heart disease (CHD) is notably absent. Resilience is the capacity to develop oneself successfully despite adverse circumstances. In a study of patients with acute coronary syndrome (ACS), the authors investigated the effect of resilience on indicators of CV severity and the physiological mechanisms underlying this effect. Patients (n=134) completed a scale measuring resilience. The authors measured troponin-I and myoglobin as indicators of ACS severity, and white blood cell (WBC) count and neutrophils as inflammatory markers. Results showed that self-efficacy-a component of resilience-was negatively related to both myoglobin and troponin after the acute coronary event. The relationship between resilience and these prognostic markers was mediated by the WBC count. Importantly, this result held significant after controlling for the effect of classic CV risk factors and demographics. The authors conclude that resilience decreases the extent of the myocardial infarction by affecting the inflammatory response, showing a protective effect.

PALABRAS CLAVE
Resiliencia;
Inflamación;
Infarto coronario agudo;
Síndrome coronario agudo;

Resumen En la actualidad la investigación sobre la influencia de los rasgos de personalidad positivos sobre la enfermedad coronaria (EC) es escasa. La resiliencia se define como la capacidad para autodesarrollarse con éxito a pesar de las circunstancias adversas. En un estudio, los autores han investigado el efecto de la resiliencia en varios indicadores de severidad en pacientes con síndrome coronario agudo (SCA; n=134) y los mecanismos que subyacen a este efecto. Los pacientes completaron una escala que medían sus niveles de resiliencia. Los autores midieron los niveles de troponina-I y mioglobina como indicadores

*Corresponding author at: Facultad de Psicología, Campus Universitario de Cartuja, s/n, 18071 Granada, Spain.
E-mail address: rretamer@ugr.es (R. Garcia-Retamero).

Estudio cross-sectional

de la severidad del SCA, y el número total de glóbulos blancos (NGB) y neutrófilos como marcadores de inflamación. Los resultados han puesto de manifiesto que el nivel de autoeficacia —un componente de la resiliencia— se relaciona negativamente con los niveles de mioglobina y troponina después de un evento coronario agudo. La relación entre la resiliencia y estos marcadores está mediada por el NGB. Este resultado se mantiene tras controlar el efecto de los factores cardiovasculares clásicos y demográficos. Los autores concluyen que la resiliencia reduce la extensión del infarto de miocardio influyendo en la respuesta inflamatoria, mostrando un efecto protector.

Cardiovascular disease (CVD) is a major public health burden in the industrialized countries, including the United States and Europe (World Health Organization [WHO], 2011). Most recent estimates from the American Heart Association suggest that one third of American adults (i.e., nearly 80 million people) have some form of CVD (Roger et al., 2012). The most common forms are: coronary heart disease (CHD), chest pain, heart failure, and stroke (Roger, Go, Lloyd-Jones, Adams, Berry, Brown, 2011). Data from prospective-cohort and case-control studies showed that modifiable risk factors (e.g., smoking, high lipid levels, obesity, physical inactivity, low daily fruit and vegetable consumption, and alcohol overconsumption) are important predictors of risk of CVD (Yusuf et al., 2004).

There is also a growing body of literature showing that psychological factors play a crucial role in adverse cardiovascular outcomes (Pelle, Denollet, Zwisler, & Pedersen, 2009). To illustrate, methodologically sound epidemiological studies indicated that negative emotions, including stress, and sub-facets of negative affectivity (e.g., depression) contribute to the initiation and progression of CVD (Denollet, Freedland, Carney, de Jonge, & Roest, 2013). People who have had heart attacks suggest stress as the cause of their disorder (Cameron, Petrie, Ellis, Buick, & Weinman, 2005). Evidence for the role of stress as a precipitating factor for heart attack in people with CVD is also clear: Stress increases risk (Arnold, Smolderen, Buchanan, Li, & Spertus, 2012). A large cross-cultural study, the INTERHEART study (Yusuf et al., 2004), compared more than 15,000 people who had experienced a myocardial infarction (MI) with almost as many who had not, attempting to identify significant risk factors that held across cultures. This study identified a set of stressors that showed a significant relationship to MI, including workplace and home stress and major life events. These stress factors were significantly related to MI and made a substantial contribution to the risk.

Depression is also a major contributor to CVD. Depression is common among individuals with heart disease especially after acute MI, with more than 1 in 5 patients meeting diagnostic criteria (Thombs et al., 2008). Depression is 3 times more common in patients after acute MI than in the general community (Thombs et al., 2006). Depression during hospitalization is associated with more than 3-fold increased risk of CHD within 18 months of the hospitalization (Dragu et al., 2008). Moreover, in a study of 5-year CHD survival among cardiac patients, Lesperance, Frasure-Smith, Talajic, and Bourassa (2002) showed that increases in the level of depression were associated with dose-response increases in CHD risk.

Interestingly, research investigating the effect of positive emotions, cognitions, and personality traits to the initiation and progression of CHD has been notably absent. In addition, the few studies on this issue did not explore possible physiological mechanisms underlying their effect (Tugade, Fredrickson, & Barrett, 2004). To illustrate, the tendency to hold optimistic beliefs about the future has been found to be associated with better cardiovascular health in some prospective studies (Tindle et al., 2009). The effects of optimistic beliefs include lower incidence of CHD and risk of cardiovascular death, and better prognosis following heart surgery (Giltay, Kamphuis, Kalmijn, Zitman, & Kromhout, 2006; Kubzansky, Sparrow, Vokonas, & Kawachi, 2001).

Another concept related to CVD that is gaining momentum is resilience-or the capacity to overcome adverse events and to be able to develop oneself successfully despite very adverse circumstances (e.g., death of family members, wars, serious traumas; Ali, Dwyer, Vanner, & Lopez, 2010; Bonanno, 2004; Seery, 2011; Zautra, Hall, & Murray, 2010). Resilience is related to the way individuals cope, overcome, and become positively strengthened by changes and challenges and has been largely studied in younger and older adults (Fry & Keyes, 2010). Resilient individuals use positive emotions to rebound from stressful experiences quickly and effectively (Giltay et al., 2006), and find positive meaning in negative circumstances.

Resilient individuals have also been found to build supportive social networks that facilitate coping, and to show a faster cardiovascular recovery after negative events (Tugade et al., 2004). For instance, Tugade and Fredrickson (2004) measured cardiovascular responding to a laboratory stressor in a sample of undergraduates. Six indices of cardiovascular responding were collected, including heart rate, finger pulse amplitude, pulse transmission times to the finger and the ear, and diastolic and systolic blood pressure. The authors calculated an aggregate index of duration of cardiovascular reactivity (time to return to baseline levels) for each participant by computing the mean duration score across these six indices, and showed that participants with higher resilience evidenced faster cardiovascular recovery from negative emotional arousal. Similarly, Chan, Lai, and Wong (2006) showed that CHD patients with higher resilience achieve better health outcomes than low-resilient CHD patients in response to an 8-week rehabilitation program, as indicated by higher physical and mental measures, lower

cholesterol levels, and better performance on a walk test. Moreover, resilience was a significant predictor of posttraumatic growth related to the onset of heart disease, indicating that CHD patients with higher resilience showed more posttraumatic growth than patients with lower resilience. However, there is a dearth of research investigating the effect of resilience on indicators of CVD severity and the physiological mechanisms underlying this effect (Feder, Nestler, Westphal, & Charney, 2010).

A number of pathophysiological mechanisms have been proposed to explain the relationship between psychological factors and cardiovascular outcomes, including hypothalamic-pituitary-adrenal axis dysregulation, platelet activation, and inflammation (Cohen et al., 2012). Circulating inflammatory markers are important predictors of cardiac risk, as they are often associated with increased incidence of adverse cardiac events (Sabatine et al., 2002) as well as increased mortality after controlling for conventional risk factors (Ikonomidis, Stamatelopoulos, Lekakis, Vamvakou, & Kremastinos, 2008). For instance, increases in interleukin (IL)-6, tumor necrosis factor alpha, and C-reactive protein play an important role in the pathogenesis and progression of CVD and are associated with various psychosocial factors including early life adversity, stress, hostility, and social isolation (Steptoe, Hamer, & Chida, 2007). The total white blood cell (WBC) count and the percentage of neutrophils are also predictors of cardiovascular outcomes (Cabrerizo-García, Zalba, Pérez, & Ruiz, 2010). In fact, a recent systematic review showed that the percentage of neutrophils measured on-admission are related to mortality rate and/or to major adverse clinical events in patients with acute coronary syndrome (ACS; Guasti et al., 2011).

Table 1 Percentage of patients with classical risk factors and ST elevation.

Variable	No	Yes	Statistical test
Smoking	84	50	χ^2=8.63, p<.01
Hypertension	57	77	χ^2=2.985, p>.08
Diabetes	87	47	χ^2=11.94, p<.01
Dyslipidemia	64	70	χ^2=.27, p>.60
ST elevation	67	67	χ^2=.00, p=1.00

In the current research, we investigated whether resilience influences cardiovascular prognosis in patients with ACS. In particular, we investigated whether resilience affects levels of troponin-I and myoglobin-two cardiac enzymes that are released to the vascular system after a myocardial infarction. These enzymes serve as sensitive and specific indicators of damage to the myocardium and tend to be reliable indicators of ACS severity in clinical practice (Thygesen et al., 2012). Peak levels of these enzymes after an acute coronary event correlate with the extension of the MI and provide important prognostic information (Heidenreich et al., 2001). We also investigated the physiological mechanisms underlying the effect of resilience on ACS severity. Following Feder et al. (2010), we examined whether this effect is mediated by inflammation (i.e., total WBC count and percentage of neutrophils). In our analyses we controlled for the effect of risk factors including age, sex, hypertension, diabetes, dyslipidemia, smoking, and body mass index (BMI).

Method

Sample

Our participants were 134 consecutive patients (average age of 61.8 years, *SD*=9.80, range 31-82; 82% males) who were admitted to the hospital "Virgen de las Nieves" of the University of Granada with ACS. Patients' sociodemographic features are displayed in Tables 1 and 2. Half of the patients had dyslipidemia and ST elevation*; one third smoked and had diabetes; and almost 60% had hypertension. Patients with or without ST-segment elevation were eligible to participate in the study. The inclusion criteria for participation were having elevated cardiac markers (i.e., Troponin-I) and having ischemia. The exclusion criterion were having an inflammatory disease and/or having neurological problems. Seventy-nine percent of the

* A ST-segment elevation myocardial infarction (STEMI) usually reflect an acute coronary occlusion and indicates a poor early-term clinical outcome, whereas a non-STEMI (NSTEMI) usually reflect a critically ill but not complete coronary artery obstruction and indicates a poor long-term clinical outcome (Park et al., 2013).

Table 2 Averages, 95% confidence intervals (CI), standard error of the mean (SEM), and median of resilience factors and biochemical markers.

Factor	Average	95% CI LL	95% CI UL	SEM	Median
Age	61.80	60.12	63.47	0.85	63.00
BMI	28.77	28.01	29.53	0.38	28.03
Troponin I	31.49	25.10	37.89	3.23	13.94
Myoglobin	496.29	370.18	622.41	63.76	200.35
WBF	10.23	9.59	10.87	0.32	9.39
Neutrophils	69.86	67.80	71.92	1.04	70.70
RS self-efficacy	59.21	57.31	61.11	0.96	62.00
RS purpose	31.14	30.12	32.17	0.52	31.50
RS Cognitive Avoidance	39.15	38.01	40.29	0.58	40.50

approached patients were eligible and agreed to participate in the study. Patients were recruited prospectively between July 2011 and December 2011 at bedside 3 days after the ACS. Patients were recruited by a trained assistant, who described the purpose of the study and answered questions. We followed the guidelines of the European Society of Cardiology for diagnosis (see ESC Guidelines, 2007) to recruit participants. The Ethics Committee of the Hospital "*Virgen de las Nieves*" of the University of Granada approved the methodology of the study. All participants signed an informed consent form to participate in the study.

Instruments and procedure

Participants' demographics, anthropometric, and laboratory data-including fasting lipid profile and serum glucose-were measured at baseline. We measured age, sex, height, and weight in all participants. All participants provided a medical history and underwent a clinical examination. Standardized questionnaires were used to determine participants' medical history, medication use, and their cardiovascular risk. Participants were classified as hypertensive if they (a) had an average systolic blood pressure of >140 mm Hg and/or a diastolic blood pressure of >90 mm Hg at rest, (b) had previous history of hypertension, or (c) were taking antihypertensive drugs. Patients were classified as diabetics if they (a) had fasting blood glucose of >126 mg/dL, (b) had previous history of diabetes mellitus, or (c) were taking insulin/oral hypoglycemics. A fasting venous sample was collected in all patients, and total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride levels were determined by standard enzymatic methods.

Resilience. Participants completed the Wagnild and Young (1993) Resilience Scale (RS), which is a 25 item Likert-type rating scale that measures degree of resilience. It includes a number of protective health factors such as self-esteem, flexibility, ability to deal with conflict, availability of external support, and familiar cohesion. The scale was translated into Spanish by skilled translators. The translated version showed very good psychometrics (Cronbach's alpha = .90). Previous research identified two (Heilemann, Lee, & Kury, 2003; Wagnild & Young, 1993) or three components (Rodríguez et al., 2009) in exploratory factor analyses. We conducted an exploratory factor analysis with principal components extraction and Varimax rotation. With resul ts consistent with previous research, we identified the following three components in this analysis (KMO=0.76, Bartlett sphericity test $p<.001$): *self-efficacy*, or the ability to cope with difficult and complex situations as well as the strength to do it (Cronbach's alpha=.86; 11 items, examples of items are "I usually manage one way or another," and "I am able to depend on myself more than anyone else"); *purpose*, or the ability to stay motivated over time and be operative (Cronbach's alpha=.75; 6 items, examples of items are "When I make plans, I follow through with them," and "I am determined"); and *meaning of life and cognitive avoidance*, or the ability to find positive aspects in life events, and to avoid dealing with situations when you cannot change them (Cronbach's alpha=.73; 7 items, examples of items are "I feel proud that I have accomplished things in life," and "I do not dwell on things that I can't do anything about"). One item ("I seldom wonder what the point of it all is") did no load in any of the three factors.

After completing this scale, participants answered other unrelated questions. These results will be reported elsewhere. Participants completed the questionnaires at bedside while they stated at the Hospital "V*irgen de las Nieves*." There were no time constraints, but the questionnaire took approximately 30 min to complete.

Biochemical markers. We measured the following markers:

1. Indicators of ACS severity. Venous samples were collected in all patients at admission, and 3, 6, and 12 h. after admission. We used standard enzymatic methods to measure peak levels of cardiac damage enzymes after the coronary event (i.e., troponin-I and myoglobin).
2. Inflammatory markers. Venous samples were collected in all patients at admission and leucocytes (i.e., total WBC count) and percentage of neutrophils were measured using standard methods.

Statistical analyses

Demographics and characteristics of the sample of participants were analyzed using descriptive statistics and χ^2 statistical tests (Table 1; see Montero & León, 2007; Ramos-Alvarez, Moreno-Fernández, Valdés-Conroy, & Catena, 2008). Biochemical markers and resilience were positively skewed (Table 2). Therefore, we computed non-parametric Spearman rho correlations.

Troponin-I, WBC count, neutrophils, and components of resilience were converted into binary variables using their corresponding medians as cut points. BMI was dichotomized by using the standard value of 25. We defined two clusters of variables: predictor variables (the three components of resilience, i.e., RS self-efficacy; RS purpose; and SRRS) and control variables (ST elevation; classical risk factors including age, sex, hypertension, diabetes, dyslipidemia, smoking, and BMI; and inflammatory markers including WBC count and neutrophils).

We conducted logistic regression analyses to test whether predictor and control variables predict severity of ACS severity (i.e., levels of troponin-I and myoglobine) (Model I). Significant predictor and control variables were then submitted to a hierarchical logistic multiple regression analysis to determine whether significant components of resilience improve the prediction of severity of ACS after including significant control variables in the equation (Model II). Odds ratios were computed to evaluate the effect size of the variables. Chi-square test and Nagelkerke R^2 were computed to evaluate improvements in predictive power when components of resilience were added to Model II. The Hosmer-Lemeshow test was used as the goodness-of-fit test of regression models.

To investigate whether the relationship between resilience and severity of ACS is mediated by inflammatory markers, we conducted mediational analyses following Preacher and Hayes (2008), with components of resilience as predictors, indicators of ACS severity as the criterion variables, and the significant inflammatory markers (i.e.,

Table 3 Correlations between psychological variables, inflammatory markers, and indicators of ACS severity.

	My	Lk	N	RS-Self Efficacy	RS-Purpose	RS-Cognitive Avoidance
Troponin I (T-I)	.84***	.44***	.30***	−.21*	−.06	−.07
Myoglobin (My)		.48***	.36***	.17+	.07	−.08
Leukocytes (Lk)			.57**	−.19*	−.06	−.08
Neutrophils (N)				−.01	.07	−.05

** p< .001; * p< .05; + p< .10.

WBF and neutrophils) as mediators. Indirect effects were tested by using an accelerated and bias corrected bootstrap procedure (5000 samples), implemented in the Preacher and Hayes' PROCESS macro. Variables were mean centered, and heterocedasticity consistent standard errors were used. In the analyses, we controlled for the effect of ECG ST deviation and classical risk factors by including these variables as covariates. Inflammatory markers were also included as moderators in the analyses to test whether they modulate (rather than mediate) the effect of components of resilience on severity of ACS. All the statistical decisions were conducted using a two-sided .05 significance level.

Results

Resilience, severity of acute coronary syndrome, and inflammatory markers

Table 3 shows the relationships between components of resilience, inflammatory markers, and indicators of ACS severity. RS self-efficacy is related to severity of ACS (troponin-I, r= −.21, p=.02, and myoglobine, r= −.17, p=.05) and WBC count (r= −.19, p=.03). In contrast, RS purpose and cognitive avoidance are not related to ACS severity or inflammatory markers. In addition, RS purpose is related to age (r=.23, p=.01) and hypertension (r=.21, p=.02). In addition, most of the classical risk factors were related to troponin I (age, r= −.22, p=.01, diabetes, r= −.23, p=.01, smoking habits, r=.19, p=.03), myoglobine (age, r= −.20, p=.02, sex, r= −.24, p=.01, diabetes, r= −.18, p=.04), and WBC count (age, r= −.25, p=.003, sex, r= −.23, p=.01). Finally, ST elevation was associated to troponin-I (r=.61, p<.001), myoglobine (r=.58, p<.001), WBC count (r=.27, p=.001), and neutrophils r=.25, p=.004).

Logistic regression on troponin-I (Model I) indicated that ST elevation, inflammatory markers, and classical risk factors accounted for a significant amount of variability (block $\chi^2_{(8)}$=65.88, p<.001, Nagelkerke R^2=.52, HL $\chi^2_{(8)}$=8.75, p=.36, 78% correct classifications). However, only ST elevation (reference category: STEMI, OR=7.90, p<.001) and WBC count (reference category: low level, OR=4.95, p=.003) were significant. The predictive power of Model II was also significant (block $\chi^2_{(8)}$=9.91, p=.002, Nagelkerke R^2=.58, HL $\chi^2_{(8)}$=13.14, p=.11, 83% correct classifications). RS self-efficacy significantly improved predictive power (reference category: High self-efficacy, OR=5.04, p=.003), indicating that patients with low RS self-efficacy tended to have higher levels of troponin-I than those with high levels of RS self-efficacy.

Logistic regression on myoglobine (Model I) indicated that ST elevation and classical risk factors accounted for a significant amount of variability (block $\chi^2_{(8)}$=57.37, p<.001, Nagelkerke R^2=.46, HL $\chi^2_{(8)}$=3.35, p=.91). Only ST elevation (reference category: STEMI, OR=7.29, p<.001), sex (reference category: female, OR=4.33, p=.03), and WBC count (reference category: low counts, OR=4.08, p=.01) were significant. The predictive power of Model II was also significant (block $\chi^2_{(8)}$=7.01, p=.01, Nagelkerke R^2=.51, HL $\chi^2_{(8)}$=12.69, p=0.12). RS self-efficacy significantly improved prediction power (reference category: High self-efficacy, OR=3.55, p=0.01), indicating that patients with low RS self-efficacy tended to have higher levels of myoglobine than those with high RS self-efficacy.

Mechanism explaining the relationship between resilience and severity of acute coronary syndrome

When WBC count was included as a mediator in the regression analysis, the relationship between RS self-efficacy and troponin-*I* remained significant (c' path= −1.72, p=.017; see Figure 1). The relationship between RS self-efficacy and WBC count (a) and between WBC count and troponin-I (b) was also significant (a= −.36, p=.04, b=2.28, p<.001). Both the total (estimate= −2.53, p=.001) and indirect effects (Bootstrap estimated effect: −.80 95% CI [−1.81, −.12]) of RS self-efficacy on troponin-I were significant. In addition, our analysis showed that WBC count act as a mediator rather than as a moderator of the relationship between RS self-efficacy and troponin-I, $F_{(1,122)}$=0.689, p>.41.

Finally, when WBC count was included as a mediator in the regression analysis, the relationship between RS self-efficacy and myoglobine was not significant (c' path= −.29, p=.52; see Figure 2). In contrast, the relationship between RS self-efficacy and leukocytes (a) and between leukocytes and troponin-I (b) were significant (a= −.35, p=.038, b=1.42, p<.001). The total (estimate= −.79, p=.04) and indirect effects of RS self-efficacy on myoglobine (Bootstrap estimated effect: −.50 95%CI [−1.07, −.08]) were significant. Again, our analysis showed that WBC count acts as a mediator rather than as a moderator of the relationship between RS self-efficacy and myoglobine, $F_{(1,122)}$=.74, p=.39.

Discussion

In this study, we aimed at investigating the influence of resilience on biological parameters of inflammation and severity in the acute setting of an ACS. Results showed that

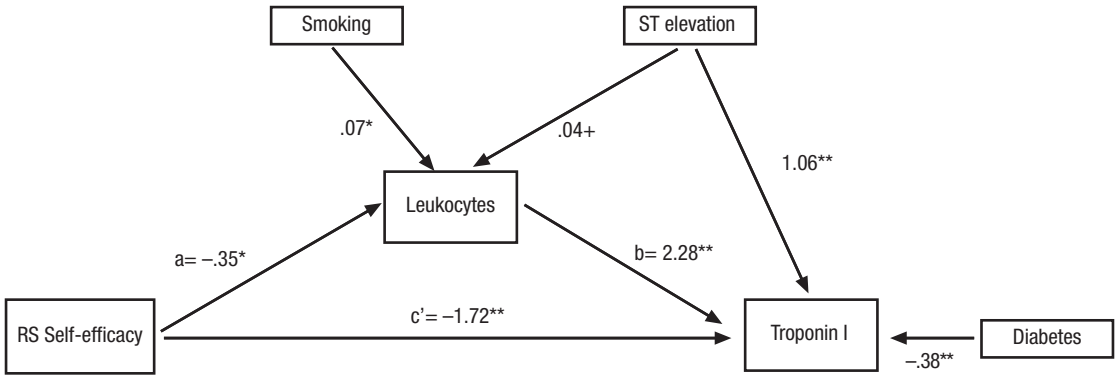


Figure 1 Path scheme of the effect of RS self-efficacy on troponin-I and the mediator effect of leukocytes. In the analyses, we controlled for the effect of ST elevation and classical risk factors. Only significant and almost significant factors were displayed. Note: Estimated coefficients are shown.
* $p < .05$, ** $p < .01$, *** $p = .09$.

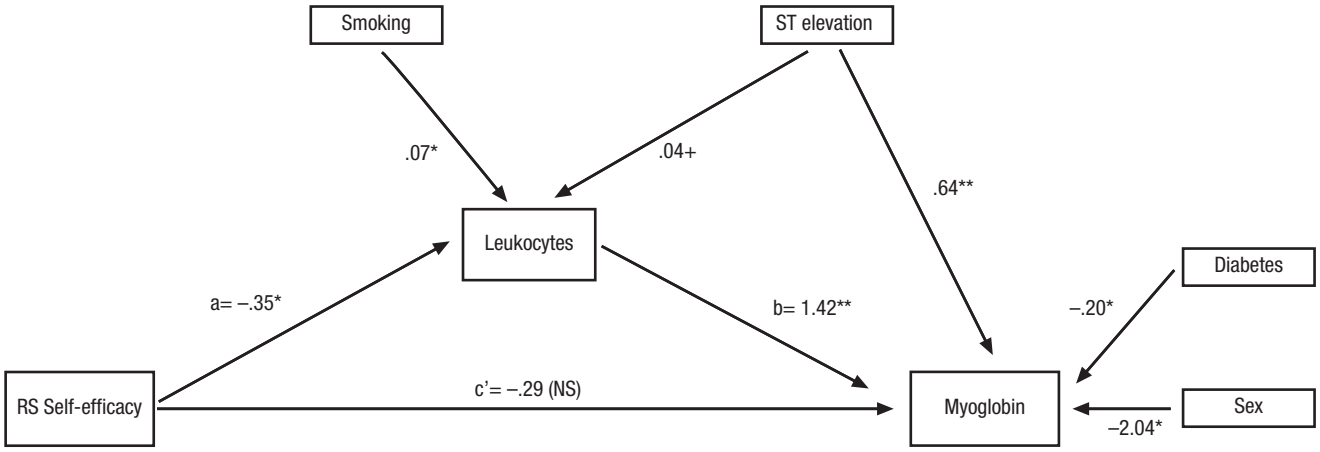


Figure 2 Path scheme of the effect of RS self-efficacy on myoglobine and the mediator effect of leukocytes. In the analyses, we controlled for the effect of ST elevation and classical risk factors. Only significant and almost significant factors were displayed. Note: Estimated coefficients are shown.
* $p<.05$, ** $p<.01$, *** $p=.09$.

self-efficacy—a component of resilience—was negatively related to peak levels of both troponin and myoglobine after an acute coronary event. Both myoglobine and troponin are important cardiac enzymes that are released after necrosis of the myocardium in the context of an acute coronary event. They are considered as prognostic markers as they reflect the magnitude of necrosis. Our results further showed that the relationship between self-efficacy and these prognostic markers was partially mediated by WBC count (i.e., an inflammatory marker). Importantly, this result held significant after controlling for the effect of ST elevation, patients' age, sex, body mass index, smoking habits, HTA, diabetes, and dyslipidemia. Thus, self-efficacy might influence the size of the myocardial infarction by affecting the inflammatory response, showing a protective effect.

Published research converges to suggest that there is a direct relationship between inflammation and coronary atherosclerosis both in acute and chronic settings (He, Tang, Ling, Chen, & Chen, 2010). Previous research (e.g., Cabrerizo-García et al., 2010; Dragu et al., 2008) also indicated that WBC count and percentage of neutrophils at admission are related to cardiovascular prognosis after an acute coronary event. In addition, Duivis et al., (2012) showed that depression predicts subsequent inflammation (e.g., leukocytes) in patients with stable CHD. In contrast, baseline levels of WBC count do not predict subsequent depressive symptoms, suggesting that depression is a risk-factor for inflammation which, in turn, predicts CHD. With our study, we add to this body of literature showing that the protective effect of resilience on CHD is also mediated by inflammation. In alignment with previous research, we assume that resilience might reduce inflammation rather than the other way around. This conclusion is supported by the fact that resilience is a personality trait relatively stable across long time periods (Bonanno, 2004; Seery, 2011; Wagnild, 2009). Therefore, it might not be influenced by transient levels of inflammation.

Our results are also consistent with research by Ikeda et al. (2011), who indicated that optimism, another positive

personality trait, also has a protective effect for CHD by reducing inflammation. In particular, the authors showed that higher overall optimism scores were associated to lower levels of interleuking-6—a cytokine with an important role in the inflammatory acute phase response. The study by Ikeda et al. (2011), however, was conducted in older men, free of CHD. Our research therefore is the first indicating that a positive personality trait tends to reduce inflammation in the context of an ACS and in turn influence the prognosis of CHD.

The potential mechanism by which psychological factors affect WBC count is not completely understood. Duivis et al., (2011) indicated that unhealthy behaviors explained the relation between depressive symptoms and the subsequent increase in the level of inflammatory cytokines in patients with stable CHD. However, these authors also showed that the relationship between depressive symptoms and levels of leukocytes were not related to levels of cytokines, BMI, waist-hip ratio, physical activity, or smoking. Therefore, the practice of health-damaging behaviors might not explain why self-efficacy influences WBC count. Other plausible explanations of this effect is the influence of chronic stress (Widmaier, Raff, & Strang, 2011), the sleep disturbance and poor sleep quality (Duivis et al., 2012), or the induction of hypercortisolemia or reduced vagal activity (Gidron, Kupper, Kwaijtaal, Winter, & Denollet, 2007). As resilience is the capacity to overcome adverse events and to be able to develop oneself successfully despite very adverse circumstances, the most plausible explanation might be that resilience reduces (i.e., has a "buffering" effect against) the negative effects of stress.

Limitations of the study

We investigated whether resilience is a protective psychological factor in CHD. The extent to what other potential protective factors (e.g., hardiness; Beasley, Thompson, & Davidson, 2003) have similar effects should be investigated in future research (Hartley, 2012). Participants in our study were a small sample of patients with ACS. Future research can also investigate whether our results hold in larger samples of healthy individuals and in patients with stable coronary heart disease. In addition, we used leukocytes (i.e., WBC count) and neurophils as an inflammatory marker. We did not investigate whether our results hold consistently in different subtypes of white blood cells (Widmaier et al., 2011; i.e. CD4 or CD8 T-cells). Future research should also investigate if some of these cell types fully mediate the relationship between resilience and severity in the acute setting of an ACS. Finally, we used a cross-sectional design in our study. Although our study can provide important theoretical insights, future search can investigate if our results hold consistently in a study using a longitudinal design.

Conclusions

Our research demonstrates that resilience decreases the size of the myocardial infarction in patients with ACS by affecting the inflammatory response. Thus, inflammation is a plausible mechanism affecting the influence that this psychological factor has on the prognosis after an acute coronary event. We hope that our study encourages future research investigating whether psychological therapy at early stages of CVD increases resilience in patients at high risk.

Funding

This research was supported by grants PSI2011-22954, to R. Garcia-Retamero and PSI2012-39292 to Andrés Catena.

References

Ali, M. M., Dwyer, D. S., Vanner, E. A., & Lopez, A. (2010). Adolescent propensity to engage in health risky behaviors: The role of individual resilience. *International Journal of Environmental Research and Public Health*, 7, 2161-2176.

Arnold, S. V., Smolderen, K. G., Buchanan, D. M., Li, Y., & Spertus, J. A. (2012). Perceived stress in myocardial infarction: Long-term mortality and health status outcomes. J*ournal of the American College of Cardiology*, 60, 1756-1763.

Beasley, M., Thompson, T., & Davidson, J. (2003). Resilience in response to life stress: The effects of coping style and cognitive hardiness. *Personality and Individual Differences*, 34, 77-95.

Bonanno, G. A. (2004). Loss, trauma, and human resilience: Have we underestimated the human capacity to thrive after extremely aversive events? *American Psychologist*, 59, 20-28.

Cabrerizo-García, S., Zalba, E. B., Pérez, C. J. I., & Ruiz, R. F. (2010). Leukocyte count as a risk factor for coronary adverse events among patients admitted for an acute coronary syndrome. *Revista Médica de Chile*, 138, 274-280.

Cameron, L. D., Petrie, K. J., Ellis, C., Buick, D., & Weinman, J. A. (2005). Symptom experiences, symptom attributions, and causal attributions in patients following first-time myocardial infarction. *International Journal of Behavioral Medicine*, 12, 30-38.

Chan, I. W. S., Lai, J. C. L., & Wong, K. W. N. (2006). Resilience is associated with better recovery in Chinese people diagnosed with coronary heart disease. *Psychology and Health*, 21, 335-349.

Cohen, S., Janicki-Deverts, D., Doyle, W. J., Miller, G. E., Frank, E., Rabine, B. S., & Turner, R. B. (2012). Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. *Proceedings of the National Academy of Sciences*, 109, 5995-5999.

Denollet, J., Freedland, K. E., Carney, R. M., de Jonge, P., & Roest, A. M. (2013). Cognitive-affective symptoms of depression after myocardial infarction: Different prognostic importance across age groups. *Psychosomatic Medicine*, 75, 701-708.

Dragu, R., Huri, S., Zuckerman, R., Suleiman, M., Mutlak, D., Agmon, Y., Kapeliovich, M., Beyar, R., Markiewicz, W., Hammerman, H., & Aronson, D. (2008). Predictive value of white blood cell subtypes for long-term outcome following myocardial infarction. *Atherosclerosis*, 1961, 405-412.

Duivis, H. E., de Jonge, P., Penninx, B. W., Na, B. Y., Cohen, B. E., & Whooley, M. A. (2011). Depressive symptoms, health behaviors, and subsequent inflammation in patients with coronary heart disease: Prospective findings from the Heart and Soul Study. *American Journal of Psychiatry*, 168, 913-920.

Duivis, H. E., Kupper, N., Penninx, B. W., Na, B., de Jonge, P., & Whooley, M. A. (2012). Depressive symptoms and white blood cell count in coronary heart disease patients: Prospective find-

ings from the Heart and Soul Study. *Psychoneuroendocrinology*. Published online. doi:10.1016/j.psyneuen.2012.07.006.

ESC Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes (2007). *European Heart Journal*, 28, 1598-1660.

Feder, A., Nestler, E. J., Westphal, M., & Charney, D. S. (2010). Psychobiological mechanisms of resilience to stress. In J. W. Reich, A. J. Zautra, & J. S. Hall (Eds.), *Handbook of adult resilience* (pp. 35-54). New York: The Guilford Press.

Fry, P. S., & Keyes, C. L. M. (2010). New frontiers in resilient aging: Life-strengths and well-being in late life. Cambridge, UK: *Cambridge University Press*.

Gidron, Y., Kupper, N., Kwaijtaal, M., Winter, J., & Denollet, J. (2007). Vagus-brain communication in atherosclerosis-related inflammation: A neuroimmunomodulation perspective of CAD. *Atherosclerosis*, 195, e1-e9.

Giltay, E. J., Kamphuis, M. H., Kalmijn, S., Zitman, F. G., & Kromhout, D. (2006). Dispositional optimism and the risk of cardiovascular death: The Zutphen Elderly Study. *Archives of Internal Medicine*, 166, 431-436.

Guasti, L., Dentali, F., Castiglioni, L., Maroni, L., Marino, F., Squizzato, A., Ageno, W., Gianni, M., Gaudio, G., Grandi, A. M., Cosentino, M., & Venco, A. (2011). Neutrophils and clinical outcomes in patients with acute coronary syndromes and/or cardiac revascularization: A systematic review on more than 34,000 subjects. *Thrombosis and Haemostas*is, 106, 591-599.

Hartley, J. (2012). New ways of making academic articles easier to read. *International Journal of Clinical and Health Psychology*, 12, 143-160.

He, L., Tang, X., Ling, W., Chen, W., & Chen, Y. (2010). Early C-reactive protein in the prediction of long-term outcomes after acute coronary syndromes: A meta-analysis of longitudinal studies. *Heart*, 96, 339-346.

Heidenreich, P. A., Alloggiamento, T., Melsop, K., McDonald, K. M., Go, A. S., & Hlatky, M. A. (2001). The prognostic value of proponin in patients with non-ST elevation acute coronary syndromes: A meta-analysis. *Journal of the American College of Cardiology*, 38, 478-485.

Heilemann, M. V., Le, K., & Kury, F. S. (2003). Psychometric properties of the Spanish version of the resilience scale. *Journal of Nursering Measurement*, 11, 61-72.

Ikeda, A., Shwartz, J. S., Peters, J. L., Fang, S., Spiro, A., Sparrow, D., Vokonas, P., & Kubzansk, L. (2011). Optimism in relation to inflammation and endothelial dysfunction in older men: The VA Normative Aging Study. *Psychosomatic Medicine*, 73, 664-671.

Ikonomidis, I., Stamatelopoulos, K., Lekakis, J., Vamvakou, G. D., & Kremastinos, D. T. (2008). Inflammatory and non-invasive vascular markers: The multimarker approach for risk stratification in coronary artery disease. *Atherosclerosis*, 199, 3-11.

Kubzansky, L. D., Sparrow, D., Vokonas, P., & Kawachi, I. (2001). Is the glass half empty or half full? A prospective study of optimism and coronary heart disease in the Normative Aging Study. *Psychosomatic Medicine*, 63, 910-916.

Lesperance, F., Frasure-Smith, N., Talajic, M., & Bourassa, M. G. (2002). Five-year risk of cardiac mortality in relation to initial severity and one-year changes in depression symptoms after myocardial infarction. *Circulation*, 105, 1049-1053.

Montero, I., & León, O. G. (2007). A guide for naming research studies in Psychology. *International Journal of Clinical and Health Psychology*, 7, 847-862.

Park, H. W., Yoon, C. H., Kang, S. H., Choi, D. J., Kim, H. S., Cho, M. C., Kim, Y. J., Chae, S. C., Yoon, J. H., Gwon, H. C., Ahn, Y. K., Jeong, M. H., & KAMIR/KorMI Registry (2013). Early- and late-term clinical outcome and their predictors in patients with ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction. *International Journal of Cardiology*, 15, 254-261.

Pelle, A. J., Denollet, J., Zwisler, A. D., & Pedersen, S. S. (2009). Overlap and distinctiveness of psychological risk factors in patients with ischemic heart disease and chronic heart failure: Are we there yet? *Journal of Affective Disorders*, 113, 150-156.

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods, Instruments, and Computers*, 40, 879-891.

Ramos-Alvarez, M. M., Moreno-Fernández, M. M., Valdés-Conroy, B., & Catena, A. (2008). Criteria of the peer review process for publication of experimental and quasi experimental research in Psychology: A guide for creating research papers. *International Journal of Clinical and Health Psychology*, 8, 751-764.

Rodríguez, M., Pereyra, M. G., Gil, E., Jofré, M., De Bortoli, M., & Labiano, L. M. (2009). Propiedades psicométricas de la escala de resiliencia versión argentina. *Evaluar*, 9, 72-82.

Roger, V. L., Go, A. S., Lloyd-Jones, D. M., Adams, R. J., Berry, J. D., & Brown, T. M. (2011). Heart disease and stroke statistics–2011 update: A report from the American Heart Association. *Circulation*, 123, e18-e209.

Roger, V. L., Go, A. S., Lloyd-Jones, D. M., Benjamin, E. J., Berry, J. D., & Borden, W. B. (2012). Heart disease and stroke statistics-2012 update: A report from the American Heart Association. *Circulation*, 125, e2-e220.

Sabatine, M. S., Morrow, D. A., De Lemos, J. A., Gibson, C. M., Murphy, S. A., Rifai, N., McCabe, C., Antman, E. M., Cannon, C. P., & Braunwald, E. (2002). Multimarker approach to risk stratification in non-ST elevation acute coronary syndromes: Simultaneous assessment of troponin I. C-reactive protein, and Btype natriuretic peptide. *Circulation*, 105, 1760-1763.

Seery, M. D. (2011). Resilience: A silver lining to experiencing adverse life events? *Current Directions of Psychological Science*, 20, 390-394.

Steptoe, A., Hamer, M., & Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: A review and meta-analysis. *Brain, Behavior, and Immunity*, 21, 901-912.

Thombs, B. D., Bass, E. B., Ford, D. E., Stewart, K. J., Tsilidis, K. K., Patel, U., Fauerbach, J. A., Bush, D. E., & Ziegelstein, R. C. (2006). Prevalence of depression in survivors of acute myocardial infarction. *Journal of General Internal Medicine*, 21, 30-38.

Thombs, B. D., De Jonge, P., Coyne, J. C., Whooley, M. A., Frasure-Smith, N., Mitchell, A. J., Zuidersma, M., Eze-Nliam, C., Lima, B. B., Smith, C. G., Soderlund, K., & Ziegelstein, R. C. (2008). Depression screening and patient outcomes in cardiovascular care: A systematic review. *Journal of the American Medical Association*, 300, 2161-2171.

Thygesen, K., Alpert, J. S., Jaffe, A. S., Simoons, M. L., Chaitman, B. R., & White, H. D. (2012). Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial. Third universal definition of myocardial infarction. *European Heart Journal*, 33, 2551-2567.

Tindle, H. A., Chang, Y. F., Kuller, L. H., Manson, J. E., Robinson, J. G., Rosal, M. C., Siegle, G. J., & Matthews, K. A. (2009). Optimism, cynical hostility, and incident coronary heart disease and mortality in the Women's Health Initiative. *Circulation*, 120, 656-662.

Tugade, M. M., & Fredrickson, B. L. (2004). Resilient individuals use positive emotions to bounce back from negative emotional experiences. *Journal of Personality and Social Psychology*, 86, 320-333.

Tugade, M. M., Fredrickson, B. L., & Barrett, L. F. (2004). Psychological resilience and positive emotional granularity: Examining the benefits of positive emotions on coping and health. *Journal of Personality*, 72, 1161-1190.

Wagnild, G. M. (2009). A review of the resilience scale. *Journal of Nursing Measurement*, 17, 105-113.

Wagnild, G. M., & Young, H. M. (1993). Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement*, 1, 165-178.

Widmaier, E. P., Raff, H., & Strang, K. T. (2011). *Vander's human physiology*. New York: McGraw-Hill.

World Health Organization, WHO (2011). *Global status report on noncommunicable diseases 2010*. Geneva: World Health Organization [accessed 12 Dec 2013]. Available from: http://www.who.int/nmh/publications/ncd_report2010/en/

Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., et al. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet*, 364, 937-952.

Zautra, A. J., Hall, J. S., & Murray, K. E. (2010). Resilience: A new definition of health for people and communities. In J. W. Reich, A. J. Zautra, & J. S. Hall (Eds.), *Handbook of adult resilience* (pp. 3-29). New York: The Guilford Press.