Title: The influence of emotion regulation on the association between depression and heart rate variability in cardiac patients

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List of all acronyms used: CHD = Coronary Heart Disease; MI = Myocardial Infarction; HRV = Heart Rate Variability; vmHRV = Vagally-mediated Heart Rate Variability; BDI-II = Beck Depression Inventory (2nd Edition); ERQ = Emotion Regulation Questionnaire; COVID-19 = Coronavirus Disease 2019; PCI = Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Grafting; BMI = Body Mass Index; ECG = Electrocardiogram; HF = High Frequency; HR = Heart Rate; ERQ-R = Emotion Regulation Questionnaire Cognitive Reappraisal score; ERQ-S = Emotion Regulation Questionnaire Expressive Suppression score.

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Abstract

Objective: Poor vagally-mediated heart rate variability (vmHRV) is a mechanism linking depression to coronary heart disease (CHD). Reduced vmHRV is also considered an index of emotion dysregulation – the frequent use of maladaptive emotion regulation strategies, one of the most important being expressive suppression – which is a key component of depression. Therefore, this study aimed to investigate the moderating role of expressive suppression in the relation between depression and vmHRV in patients with CHD.

Methods: The sample included 235 patients with CHD (mean age = 61.56 years (SD = 9.80); 12% women) admitted to cardiac rehabilitation after a cardiac intervention. The Beck Depression Inventory-II (BDI-II) was administered to assess depressive symptoms. Emotion regulation strategies based on either expressive suppression or cognitive reappraisal were assessed through the Emotion Regulation Questionnaire (ERQ). Resting electrocardiographic recordings were collected for five minutes to compute HRV indices.

Results: Expressive suppression moderated the relation between depressive symptoms and vmHRV (b = -0.03; p = .012). Patients with lower expressive suppression scores showed no association between depressive symptoms and vmHRV (b = -0.00, p = .94), whereas those with higher expressive suppression scores showed a significant negative association between depressive symptoms and vmHRV (b = -0.05, p = .015).

Conclusions: The use of expressive suppression is likely to potentiate the relation between depressive symptoms and poor vmHRV, which could increase the cardiac risk in these patients. Targeting emotion regulation skills in cardiac rehabilitation programs may be useful for reducing the impact of depression in cardiac patients.

Keywords: depression, coronary heart disease, emotion regulation, expressive suppression, heart rate variability, cardiac vagal tone.

Introduction

Depression and coronary heart disease (CHD) have a huge impact on public health, being among the top five leading causes of the global burden of disease (1). Depression has an estimated prevalence of 5% in the general population (2), reaching 20% among cardiac patients (3) and approximately 45% in patients after a myocardial infarction (MI) (4). Also, it has been reported that depressive symptoms are associated with a 60% greater likelihood of exhibiting CHD (5). Major depressive disorder was recognized as a predictor of poor prognosis following a cardiac event (6-9) and of mortality risk in MI patients, increasing up to 4-fold the death rate (10). Moreover, a dose-response relation was found between the increased depression severity and subsequent cardiac events, with more severe depression associated with earlier and more severe cardiac events (11, 12). Thus, depression has been recognized as an independent risk factor for CHD onset, development and outcomes (5, 11, 13, 14). Interestingly, evidence shows that preoperative depression is the strongest predictor of postoperative depression in patients who underwent cardiac surgery (15, 16). The literature investigating the potential mechanisms linking depression to CHD (17, 18) suggests common causal pathways (19, 20). Hypothalamic-pituitary-adrenal axis hyperactivity (21), altered inflammatory response (22), high platelet aggregability (23), and autonomic nervous system imbalance (24) have been considered as the most important biological mechanisms underlying the relation between depression and increased cardiac risk.

In the last two decades, research has shown a growing interest in the analysis of variations in the time between adjacent heartbeats (Heart Rate Variability, HRV), because it provides a valuable measure of autonomic activity on the heart (25). Decreased parasympathetic tone as measured by low vagally-mediated HRV (vmHRV), has been associated with an increased risk of arrhythmia and sudden cardiac death (26, 27). Moreover, reduced vmHRV has been consistently reported in cardiac patients (28-30) and has been associated with higher cardiac risk (31-33) as well as with the negative impact of cardiac disease (9, 34).

VmHRV has also been proposed as an index of the ability of the individual to adapt to

environmental requests (35-37) which is at the basis of cardiac risk. In line with this hypothesis, autonomic control on the heart is known to be directly and indirectly modulated by a complex network of neural structures involved in high level cognitive and emotional regulation, such as the central autonomic network, including the insular cortex, amygdala, ventrolateral medulla and the medial and ventromedial prefrontal cortex (36). For these reasons vmHRV is thought to mirror cognitive and emotional flexibility, the core features underlying emotion regulation (38, 39). Specifically, emotion regulation – the ability to modify magnitude, duration and expression of an emotional response (40) – is considered an important function for a successful adjustment. Emotion dysregulation, conversely, is considered a relevant transdiagnostic factor for several psychopathological conditions, including clinically significant depression (41, 42).

Depression is characterized by excessive and persistent negative emotions, therefore it has been suggested that a dysfunction in emotion regulation may play a central role in the onset of depressive symptoms, as supported by growing evidence (43-46). According to the process model of emotion proposed by Gross (1998), there are two commonly used strategies for down-regulating emotion, namely cognitive reappraisal, and expressive suppression. Depression has been associated with the use of expressive suppression (47), which is a response-focused strategy that involves the inhibition of emotion-expressive behavior (48, 49). Regarding cognitive reappraisal, it is an antecedent-focused strategy that aims at changing the meaning of a situation to modulate its emotional impact and is considered an adaptive emotion regulation strategy, effective in mood regulation (49, 50). Indeed, a negative association was found between cognitive reappraisal and depression (51, 52). Instead, expressive suppression was reported to be less effective, compared to cognitive reappraisal, in decreasing the physiological and experiential aspects of negative emotions (50). Consistent with these findings, the use of expressive suppression was shown to correlate with the severity of depressive symptoms (53) and with long-term negative effects on life satisfaction, wellbeing, and self-esteem (49, 54). In addition, individuals who use expressive suppression (also called suppressors) were found to be more prone to experience depressive symptoms than those who

use cognitive reappraisal (49, 55).

Furthermore, altered emotional responses were found to be associated with an increased risk and impact of cardiovascular disease (9, 34). Intriguingly, increased levels of expressive suppression were reported to partially mediate the effect of depressive symptoms on postoperative vmHRV in cardiac patients (56). Such evidence highlights the importance of emotion regulation strategies training for patients with depression (57). However, to date only a few studies have investigated the relation between expressive suppression and vmHRV, showing inconclusive results (58-60). Two studies reported no significant association between self-reported use of expressive suppression and vmHRV (58, 59). Nevertheless, a recent study by Jentsch et al. (60) showed that the use of suppression during an emotion regulation task led to lower cardiac vagal flexibility as compared to cognitive reappraisal. Specifically, participants who used expressive suppression displayed smaller decreases in vagal tone during an induced stress condition, as well as less pronounced recovery in the aftermath of stress. Therefore, further studies are needed to better understand the mechanisms underlying the relation between expressive suppression and vmHRV.

In light of these considerations, the present study aimed to investigate the role of emotion regulation strategies in the relation between depressive symptoms and vmHRV in a sample of patients with CHD admitted to cardiac rehabilitation. It was hypothesized that individuals using expressive suppression would display a stronger inverse association between depressive symptoms and vmHRV compared to those who were lower in expressive suppression. Moreover, given that consistent evidence on the relation between cognitive reappraisal and depression is lacking, no hypotheses were formulated for what concerns the role of cognitive reappraisal.

Methods and materials

Participants

This study is a part of an extensive, multi-center research project including the Unit of Cardiac Rehabilitation, ULSS 6 Euganea (Padua, Italy) and the Unit of Cardiac Rehabilitation, San Marco

Hospital (Venice, Italy). The project was approved by the local ethics committees (Nucleo di Ricerca Clinica - AULSS 6 Euganea, prot. No. 209498; Comitato Etico Sperimentazione Clinica Provincia di Venezia e IRCSS San Camillo (CESC), prot. No. 5137B6558BA9E00C7BE4CBFD4FED0BFA; Comitato Etico Della Ricerca Psicologica (AREA 17), prot. No. 2229). Part of the sample included in this study was described in a recent publication (60); however, data presented in this study are previously unpublished. Data collected at San Marco Hospital (Venice, Italy) were excluded from this study because patients were recruited at the end of primary cardiac rehabilitation, whereas patients from ULSS 6 Euganea (Padua, Italy) were enrolled at the beginning of secondary cardiac rehabilitation.

After receiving approval from the local ethics committee, 385 patients admitted to the Unit of Cardiac Rehabilitation of Padua were proposed to participate in the study between December 2017 and February 2020, before the coronavirus disease 2019 (COVID-19) emergency in Italy (see Figure 1).

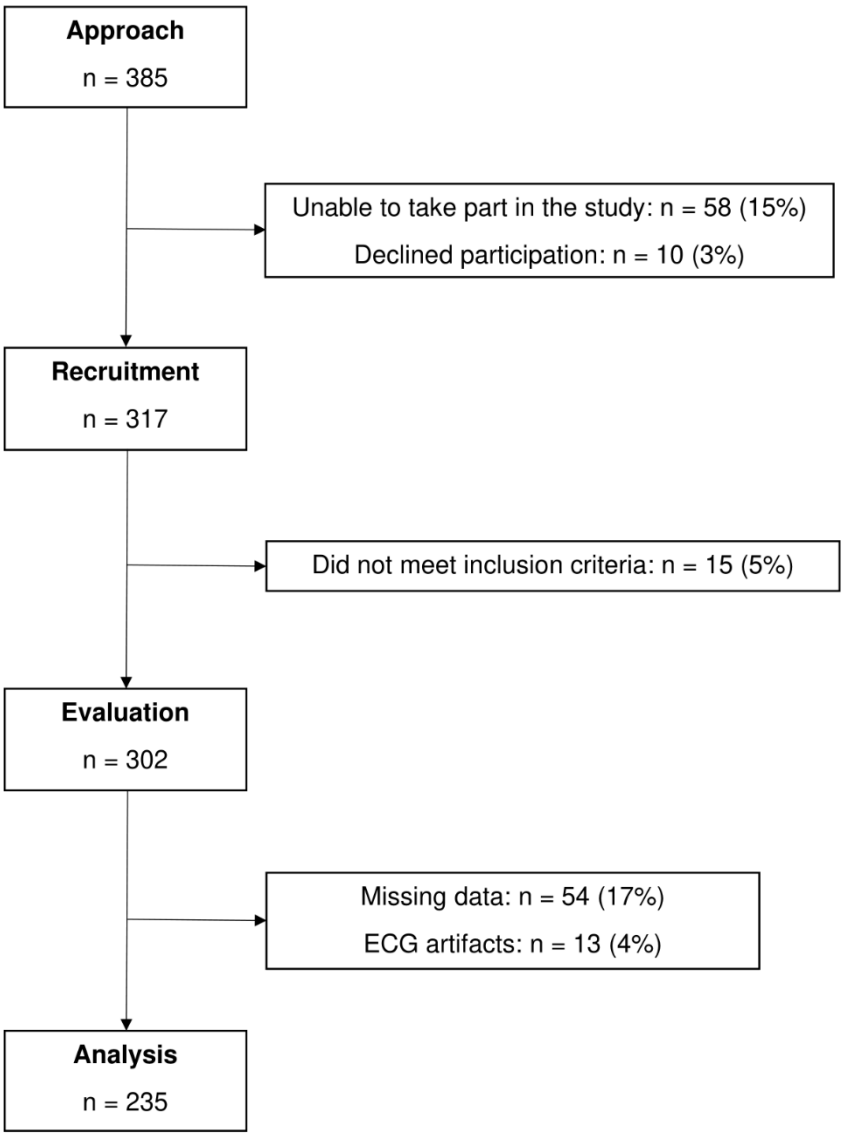

Figure 1: STROBE diagram. STROBE diagram of patients' enrolment from the first contact to the data analysis.

Of those, 58 (15%) were unable to take part in the study and 10 (3%) declined participation. Thus, 317 patients were enrolled in the study. Exclusion criteria were inability to read or to understand Italian; visual or auditory impairments; incomplete data collection; conflicting research protocol; a history of severe psychiatric illness; life-threatening condition; cardiac arrhythmia; a history of symptomatic cerebrovascular disease and/or neurological deficit as obtained from patient's medical

158 records and confirmed by medical staff. Eighty-one patients were excluded because of the presence
159 of cardiac arrhythmia (n = 15, 5%), incomplete data collection (n = 54, 17%) or artifacts in the
160 electrocardiographic (ECG) recording (n = 13, 4%). Thus, the final sample consisted of 235 patients,
161 mostly males (n = 208, 88%), with a mean (SD) age of 61.56 (9.80) years. Most patients (n = 195,
162 83%) underwent percutaneous coronary intervention (PCI), 40 (18%) underwent cardiac surgery
163 (specifically, 20 (9%) underwent coronary artery bypass grafting (CABG) and 20 (9%) had a heart
164 valve replacement). Characteristics of the sample are reported in Table 1.

Table 1. Sociodemographic, biomedical and pharmacological data.

	Mean (SD) or N (%)
Age (years)	61.56 (9.80)
Education (years)	12.32 (4.06)
BMI (kg/m^2)	26.66 (3.51)
Male, N (%)	208 (88)
Walking time in a week (minutes)	226 (266)
Smoking	
Actual, N (%)	61 (26)
Past, N (%)	92 (39)
Hypertension, N (%)	165 (70)
Dyslipidemia, N (%)	147 (63)
Diabetes, N (%)	40 (17)
Myocardial infarction, N (%)	194 (85)
Days from intervention	28.68 (30.48)
History of cardiovascular events, N (%)	163 (71)
Intervention	
PCI, N (%)	195 (82)
Surgery, N (%)	40 (18)
Pharmacological therapy	
Anticoaugulants, N (%)	230 (98)
Beta-blockers, N (%)	182 (77)
ACE inhibitors, N (%)	102 (43)
Antiarrhythmics, N (%)	13 (5)
Anti-hypertensives, N (%)	65 (28)
Statins, N (%)	185 (79)
Psychotropic drugs, N (%)	9 (4)

The table shows the mean (SD) for continuous variables and frequency (%) for categorical variables. BMI = Body Mass Index; PCI = Percutaneous Coronary Intervention.

Procedure

The assessment was performed for each patient on the first day of rehabilitation at the Unit of Cardiac Rehabilitation, ULSS 6 Euganea (Padua, Italy). The procedure was administered individually by a trained psychologist in a quiet and isolated room. First, an interview assessing sociodemographic variables (age, sex, and education), and lifestyle habits – including smoking and physical activity, defined as walking time in the previous week – was conducted. Afterwards, the physiological recording took place. After the placement of electrodes and a 10-minutes adaptation to the sensors, the ECG was recorded at rest for five minutes. Participants were instructed to stay still and avoid talking during the recording. Then, the Beck Depression Inventory-II (BDI-II) and the Emotion Regulation Questionnaire (ERQ) were administered to assess the severity of depressive symptoms and the use of emotion regulation strategies, respectively. Finally, patients' medical data were collected from the medical records, including body mass index (BMI), type of intervention, days from intervention, history of cardiovascular events, cardiac risk factors (i.e., hypertension, dyslipidemia, diabetes, and arrhythmia), and pharmacological treatment (i.e., anticoagulants, beta-blockers, ACE-inhibitors, anti-hypertensives, antiarrhythmics, statins and psychotropic drugs).

Materials

Psychological assessment

In order to measure the severity of depressive symptoms, the Beck Depression Inventory-II (BDI-II) was employed (62, 63). Each of the 21 items is composed of a group of statements that refer to a specific symptom of depression (e.g., punishment feelings, loss of interest) as defined in the Diagnostic and Statistical Manual of Mental Disorders-IV (64). The statements are scored on a scale value from 0 to 3 (scores range from 0 to 63) depending on their level of severity, with a higher sum of scores suggesting more severe symptoms. Patients are asked to read each statement and choose the one that better depicts how they have been feeling during the past two weeks, including the day being. Cronbach's alpha for the BDI-II was $\alpha = .85$.

In order to assess individual differences in the use of emotion regulation strategies, the Emotion Regulation Questionnaire (ERQ) was administered to each patient (65). The scale is designed to measure the respondents' tendency to use cognitive reappraisal and expressive suppression as strategies to regulate emotional responses. Cognitive reappraisal is an antecedent-focused strategy based on the re-evaluation of an emotion-eliciting situation, whereby changing the way one thinks about the event so that its impact is changed. On the other hand, expressive suppression is a response-focused strategy, implemented when the emotional response has fully developed, that aims at reducing the experiential and behavioral aspects of negative emotions. The scale is composed of 10 different statements that refer to emotional experience and expression, particularly to how emotions are controlled and regulated in respect to the two considered strategies (e.g., "I control my emotions by changing the way I think about the situation I'm in", "I keep my emotions to myself"). Respondents are asked to indicate their level of agreement on a Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). The measure provides two scores, one for each subscale: cognitive reappraisal (ERQ-R), which consists of 6 items, and expressive suppression (ERQ-S), which involves 4 items. A greater score, which is the mean of scores for each subscale (ranging from 1 to 7) indicates a greater endorsement of the emotion regulation strategy. Cronbach's alpha for the ERQ-R and ERQ-S subscales was α =.83 and α = .73, respectively.

Electrocardiographic recording

The ECG signal was acquired with disposable Ag/AgCl electrodes positioned according to the lead II Einthoven's configuration. ECG was recorded at rest for five minutes; the signal was band-pass filtered (1-100 Hz) and sampled at 256 Hz. ECG recordings were visually inspected, and artifacts (e.g., ectopic beats) were corrected with a piecewise cubic spline interpolation method that generates missing or corrupted values into the normal-to-normal (NN) intervals. Then, inter-beat intervals and mean heart rate (HR) were computed using R-peak detection. Frequency-domain indices were obtained through autoregressive (AR) spectral analysis using Kubios HRV Analysis software 2.2

(Matlab, Kupio, Finland).

High frequency (HF) power (0.15 - 0.40 Hz) in ms^2 has been shown to be a reliable measure of the modulation of the parasympathetic branch through the vagus nerve on the sinoatrial node in response to both internal and external challenges (66-69). Indeed, HF power is considered an index of vagal control on the heart. For these reasons, HF power was chosen as a reliable index of vmHRV. In line with current recommendations (69), HF power was natural log-transformed to fit the assumptions for linear analyses.

Data analysis

Data analysis was conducted in R (70). Descriptive statistics have been calculated for each variable of interest. Pearson's product moment correlation coefficients were calculated to explore the relations among each psychological (BDI-II, ERQ-R and ERQ-S scores) and physiological (heart rate and vmHRV, as reflected by lnHF power) measure. In order to investigate the influence of the use of beta-adrenergic blocking agents, the Mann-Whitney U test was conducted on HR and vmHRV, comparing patients who were and who were not receiving beta-blockers. Then, to examine the role of the use of emotional regulation strategies as a possible moderator of the relation between depressive symptoms and vmHRV, a two-stage hierarchical regression analysis examining moderation effects was conducted with the lnHF power as the dependent variable. ERQ-R and ERQ-S scores, as well as the continuous score of the BDI-II, were entered in block 1 of the hierarchical regression along with five covariates, specifically age, sex, BMI, type of cardiovascular intervention (i.e., surgery or PCI), and physical activity. Two-way interactions between ERQ-R and ERQ-S as moderator variables and BDI-II as the independent variable were entered in block 2. To improve the interpretation of results, the independent and the moderator variables were mean-centered. Multicollinearity diagnostics were run using the mctest package (71), showing acceptable levels of collinearity (72) among the variables entered in the model (variance inflation factor <4, tolerance >0.03 and condition index <30). To probe the interaction effect, Johnson-Neyman interval (73) was calculated using the interactions package

(74). The Johnson-Neyman interval calculation was used to create a dummy variable that categorized patients into two levels of ERQ-S, therefore creating two groups: 1) high ERQ-S; and 2) low ERQ-S. Then, a simple slope analysis was performed on a model including the lnHF as the dependent variable, the ERQ-S group as the moderator variable, and the BDI-II as the independent variable. Given that evidence from previous studies was insufficient to estimate the effect size, it was not possible to conduct an a priori power analysis. However, a post-hoc power analysis was performed using G*power (75), version 3.1.9.6 (Universität Kiel, Germany) to assess the power of this study for the observed effect size. For this assessment, the recommended effect sizes were as follows: f^2 = .02 for small effects, medium f^2 = .15 for medium effects, and f^2 = .35 for large effects (76). The statistical type I two-sided (alpha) level was fixed at α <.05.

Results

Characteristics of the sample

The mean (SD) BDI-II score of our sample was 7.3 (5.9), with an observed range of 0 to 35. 204 (87%) patients showed minimal depressive symptoms (BDI-II ranging from 0 to 13), 21 (9%) patients reported mild depressive symptoms (BDI-II ranging from 14 to 19), 8 (3%) patients had moderate depression scores (BDI-II ranging from 20 to 28) and 2 (1%) reported severe depressive symptoms (BDI-II ranging from 29 to 63). The mean (SD) ERQ-S score was 3.9 (1.5), with an observed range of scores from 1 to 7. The ERQ-R score had a mean (SD) value of 5.0 (1.2) and an observed range of scores of 1 to 7. The mean (SD) heart rate was 62.4 (11.36) beats/min, ranging from 36.1 to 108.4 beats/min. With respect to lnHF power, the mean (SD) was 4.8 (1.4) with observations ranging from 0.6 to 8.0. For illustrative purposes boxplots of HR and lnHF have been realized. Specifically, the sample was divided into four groups based on combined median-split performed firstly on BDI-II and ERQ-R scores and secondly on BDI-II and ERQ-S scores (See Figure S1, Supplemental Digital Content 1). As expected, the Mann-Whitney U test showed a significant difference in mean HR between patients who were and who were not taking beta-blockers (W = 5811.5, p = .023).

Conversely, no significant difference in vmHRV was found between the two groups (W = 4356, p = .37).

Association among physiological and psychological measures

Pearson's correlation test showed a significant association between the BDI-II score and HR (r = .20, p = .002). Specifically, the greater the severity of depressive symptoms, the higher the HR. A significant correlation was also found between the BDI-II and the ERQ-S score (r = .16, p = .012), with greater severity of depressive symptoms being associated with higher use of expressive suppression. Moreover, a significant positive correlation was found between ERQ-S and ERQ-R scores (r = .16, p = .012). Furthermore, the BDI-II score was marginally significantly correlated with vmHRV (r = -.12, p = .061). In contrast, no significant correlation was found between the BDI-II and the ERQ-R. Also, no significant correlations were found between the physiological measures (vmHRV and HR) and the self-report emotion regulation strategies (ERQ-S and ERQ-R scores). Pearson's correlations among each psychological and physiological measure are reported in Table S1, Supplemental Digital Content 2.

The moderating role of expressive suppression

In block 1 the hierarchical regression for moderation effects (see Table 2) showed that the BDI-II score was significantly associated with vmHRV (p = .032), with more severe depressive symptoms being correlated with lower vmHRV. Conversely, no significant association was found between vmHRV and ERQ-R (p = .67) or ERQ-S (p = .27) scores. The regression analysis also showed a significant relation between the type of intervention and vmHRV (p < .001). Specifically, lower vmHRV was observed in patients who underwent surgical intervention (i.e., CABG or heart valve replacement) as compared with those who underwent PCI.

With respect to block 2 of the model, the ERQ-S × BDI-II interaction was significantly associated with vmHRV (p = .012). Conversely, the BDI-II, ERQ-R, and ERQ-S scores were unrelated to vmHRV.

299 Moreover, the ERQ-R × ERQ-S, and ERQ-R × BDI-II interactions were unrelated to vmHRV (see
300 Table 2). In block 2, a significant association was found between vmHRV, and type of intervention (p <
301 .001), consistent with the results observed in block 1. Furthermore, a significant relation between the
302 BMI and vmHRV was found (p = .047). The overall model fit was R^2 = 0.11 with an effect size of f^2 =
303 0.18, hence the power of this study was more than adequate to detect the effect of the model, being
304 (1-β) = 0.99.

Table 2. Hierarchical regression analysis on vmHRV.

Block	Predictor	*b*	confidence interval (95%)	*t* value	*p*	
1						
	(Intercept)	7.25	[5.23, 9.26]	7.08	<.001	***
	Age (years)	-0.01	[-0.03, 0.00]	-1.57	.12	
	Sex (*0 = male; 1 = female*)	0.28	[-0.28, 0.84]	0.98	.33	
	BMI (kg/m^2)	-0.05	[-0.10, 0.00]	-1.78	.076	
	Walking time in a week (minutes)	-0.00	[-0.00, 0.00]	-0.68	.50	
	Intervention (*0 = PCI, 1 = surgical intervention*)	-1.18	[-1.66, -0.70]	-4.86	<.001	***
	ERQ-R	-0.03	[-0.18, 0.12]	-0.42	.67	
	ERQ-S	0.07	[-0.05, 0.19]	1.12	.27	
	BDI-II	-0.03	[-0.06, -0.00]	-2.16	.032	*
2						
	(Intercept)	7.27	[5.27, 9.27]	7.17	<.001	***
	Age (years)	-0.01	[-0.03, 0.78]	-1.27	.21	
	Sex (*0 = male; 1 = female*)	0.22	[-0.33, 0.78]	0.80	.43	
	BMI (kg/m^2)	-0.05	[-0.10, -0.00]	-1.99	.047	*
	Walking time in a week (minutes)	-0.00	[-0.00, 0.00]	-0.67	.50	
	Intervention (*0 = PCI, 1 = surgical intervention*)	-1.24	[-1.72, -0.75]	-5.05	<.001	***
	ERQ-R	-0.04	[-0.19, 0.12]	-0.45	.65	
	ERQ-S	0.05	[-0.07, 0.18]	0.87	.39	
	BDI-II	-0.03	[-0.06, 0.00]	-1.73	.085	
	ERQ-R × ERQ-S	-0.03	[-0.12, 0.06]	-0.59	.55	
	ERQ-R × BDI-II	0.00	[-0.02, 0.03]	0.35	.73	
	ERQ-S × BDI-II	-0.03	[-0.04, -0.00]	-2.55	.012	*

Note: BMI = body mass index; PCI = Percutaneous Coronary Intervention; BDI-II = Beck Depression Inventory (2nd edition); ERQ-R = Emotion Regulation Questionnaire – Cognitive Reappraisal score; ERQ-R = Emotion Regulation Questionnaire – Expressive Suppression score; vmHRV = vagally-mediated Heart Rate Variability. *** = p <.001, ** = p <.01, * = p < .05

The results of the Johnson-Neyman calculation showed that when ERQ-S score was outside the interval i = [-38.9, 4.20], the slope of the BDI-II was significant at a fixed α = .05. More specifically, the BDI-II score had a significant inverse association with vmHRV in patients with ERQ-S scores higher than 4.2. Instead, in patients with ERQ-S scores lower or equal than 4.2, no significant association between the BDI-II and vmHRV was observed (see Figure 2a). Based on the Johnson-Neyman interval, a dummy variable was created to categorize patients as those with low expressive suppression (ERQ-S score ≤ 4.2; n = 114, 49%) and those with high expressive suppression (ERQ-S score > 4.2; n = 121, 51%). The simple slopes analysis showed an inverse linear association between BDI-II scores and vmHRV in patients with high ERQ-S (b = -0.05, t(233) = -2.45, p = .01). Conversely, patients with low ERQ-S scores showed no significant association between BDI-II and vmHRV (b = -0.00, t(233) = -0.07, p = .94; see Figure 2b).

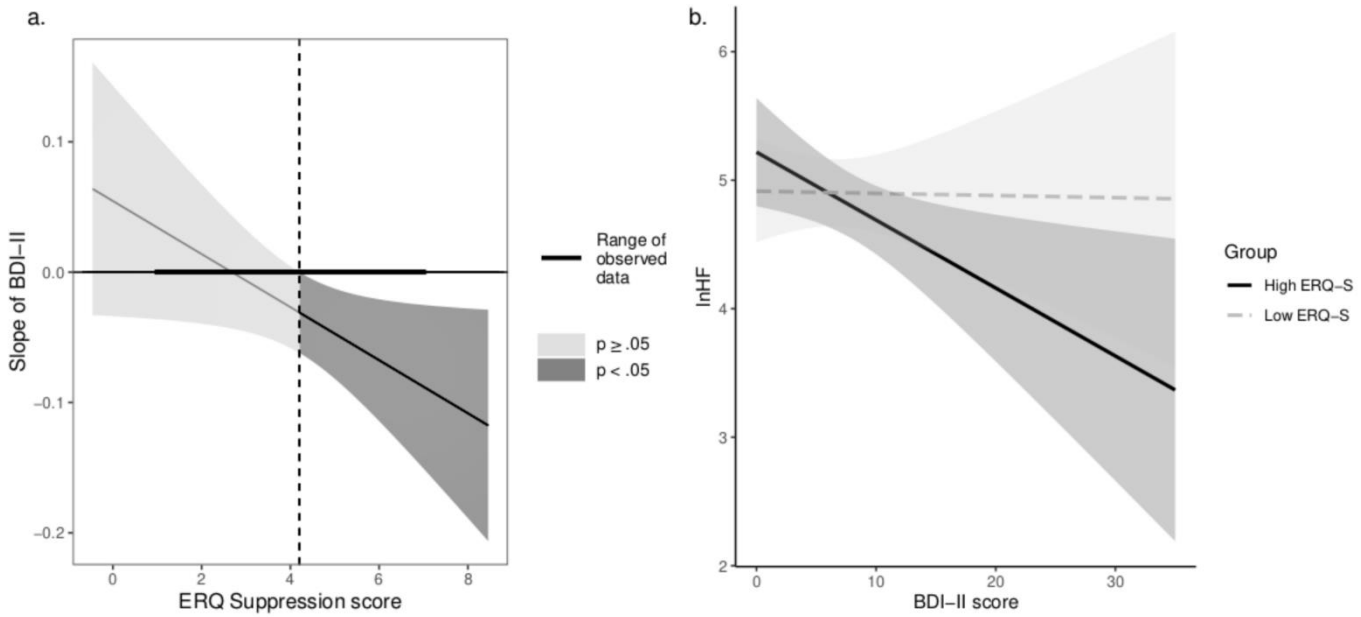

Figure 2: The moderating role of expressive suppression. Figure 2.a *Johnson-Neyman interval plot.* The dark grey part of the curve represents the range of expressive suppression values (ERQ-S scores) at which the slope of BDI is significant at a fixed α = .05. Patients with lower ERQ-S scores (ranging from the minimum to 4.2) showed no significant relation between depressive symptoms and vmHRV, while patients with higher expressive suppression values (ERQ-S scores > 4.2) showed a significant association between depressive symptoms and vmHRV ($p < .05$). Figure 2.b *Moderation model of ERQ-S between the BDI-II and vmHRV*. The plot displays the moderation effect of expressive suppression (ERQ-S) on the association between depressive symptoms (BDI-II scores) and vmHRV. The black line represents the significant negative association between BDI-II and vmHRV in patients with high ERQ-S, while the dashed light grey line represents patients with low ERQ-S.

Discussion

The main aim of the present study was to investigate the moderating effect of maladaptive emotion regulation, specifically expressive suppression, in the relation between depression and vmHRV in a group of patients with CHD. It was expected that greater use of suppression would potentiate the association between more severe depressive symptoms and reduced vmHRV. In line with this hypothesis, the results showed a significant moderating role of the maladaptive ER strategy in the relation between depression and vmHRV (as indexed by lnHF power). Specifically, only patients who were more prone to use expressive suppression to cope with their emotions showed a significant inverse association between the severity of depressive symptoms and vmHRV. In contrast, those who did not use expressive suppression as a preferential emotion regulation strategy displayed no association between depressive symptoms and vmHRV. Consistent with previous findings (47), expressive suppression was also found to be related to depression, with higher self-reported use of expressive suppression being associated with more severe depressive symptoms. Furthermore, vmHRV was found to be inversely related to depressive symptoms, showing lower vmHRV in those with more severe depressive symptoms, in line with evidence from previous studies (77). Ultimately, an association was found between mean HR and depression, as higher HR was associated with more severe depressive symptoms, in accordance with prior results (78).

Instead, cognitive reappraisal was unrelated to vmHRV. This null finding is in contrast with evidence from previous studies conducted on healthy individuals (79-81), reporting a positive correlation between cardiac vagal tone and the use of cognitive reappraisal. Therefore, further research is needed to investigate whether the relation between cardiac vagal tone and cognitive reappraisal may extend to clinical populations. Furthermore, cognitive reappraisal was unrelated to depressive symptoms and was found to have no effect on the relation between depressive symptoms and vmHRV. These findings are in line with previous evidence showing null to moderate associations between cognitive reappraisal and depression (82, 83).

Taken together, the present results suggest that expressive suppression, compared to cognitive

362 reappraisal, may be more relevant and specific when it comes to the influence of emotion regulation
363 on the link between depressive symptoms and vagal cardiac modulation. Furthermore, expressive
364 suppression could sustain depression-related cardiac risk by strengthening the link between vmHRV,
365 altered neurohormonal responses and depressive symptoms. Such evidence highlights the
366 importance of an integrative approach to cardiovascular risk, considering emotion regulation strategies
367 as they may provide additional and valuable information. The literature shows that targeting
368 depressive symptoms through both psychotherapeutic and pharmacological interventions has a
369 positive effect on cardiovascular outcomes (84). The assessment of emotion regulation skills could be
370 useful to identify patients with CHD who are at higher depression-related cardiac risk and to develop
371 specific interventions aimed at reducing the use of expressive suppression and, ultimately,
372 depression. Thus, an integrated intervention that targets vmHRV (such as HRV-biofeedback training)
373 and emotion regulation skills could reduce the impact of depression and emotion dysregulation on
374 cardiovascular risk and prognosis, as suggested by previous evidence (85), by improving autonomic
375 balance and emotional adaptation. Indeed, HRV-biofeedback is considered an effective tool for
376 enhancing emotional self-control, reducing depressive symptoms, and facilitating psychological
377 adjustment to CHD (86, 87). Furthermore, mindfulness-based interventions have shown promising
378 outcomes when it comes to emotion regulation (88). Growing evidence shows that mindfulness is
379 effective in reducing worry, rumination, and suppression (89), as well as depressive symptoms (90, for
380 a review see 91).

381 The present study also showed an association between the type of intervention and vmHRV.
382 Specifically, patients who underwent cardiac surgery, such as CAGB or heart valve surgery, were
383 characterized by lower vmHRV as compared with those who underwent PCI. This result is consistent
384 with those of previous studies showing that restored myocardial perfusion by PCI in patients with CHD
385 is followed by an improvement of HRV indices (92, 93). CABG and heart valve surgery, involving more
386 invasive procedures than PCI, are likely to have a deeper impact on patients' recovery, which is also
387 reflected by reduced HRV levels (94, 95). Moreover, regression analysis revealed a relation between

BMI and vmHRV, with higher BMI being associated with lower vmHRV, in line with extensive literature (96, 97).

In the present study, participants showed a lower prevalence of depression as well as milder depressive symptoms compared to similar studies. Specifically, 13% of our sample showed mild to severe depressive symptoms, while data from previous studies suggests that the prevalence of depression in patients with CHD is approximately 20-25% (6, 98). This difference can be accounted for by considering that this study was conducted on a sample of patients with CHD who mainly underwent PCI intervention (82%). Indeed, patients enrolled in the present study may have experienced a faster recovery compared to other cardiac patients, thus showing mild depressive symptoms. The present study assessed mechanisms that have been mainly investigated in patients undergoing CABG intervention, being subjected to a worse prognosis, slower recovery, and more severe depressive symptoms (98). Therefore, the present study extends the generalizability of the link between expressive suppression and depressive symptoms in patients with CHD to populations subjected to more subtle symptoms.

Some limitations should be considered when interpreting the result of this study. First, the majority of patients included in the present study were males; this may reduce the generalizability of the results to females. It has also been shown that emotion regulation is subject to gender differences such as greater use of expressive suppression in men in respect to women (49). For these reasons, future studies are warranted to evaluate the relation between emotion regulation, depression and vmHRV in women. Second, given the absence of a control group suffering from other chronic diseases (e.g., diabetes), it is not possible to determine whether this relation is specific to cardiac patients, or it extends to a broader population. The third limitation resides in the use of self-report measures to assess emotion regulation strategies, depressive symptoms, and physical activity: self-reports are subject to biases and methodological caveats that could partially limit the reliability of the present study (99). Future research should use ambulatory tools, such as the actigraph accelerometers, in order to have more ecological and objective measures than self-reports. However,

with respect to the evaluation of depressive symptoms and emotion regulation strategies, it should be noted that both the BDI-II and the ERQ have demonstrated high reliability and construct validity (100, 101). In addition, 77% of the patients involved in this study were using beta-adrenergic blocking agents, which might have influenced the current findings. However, sensitivity analyses (unadjusted for covariates) revealed the same pattern of results when analyzing data on patients not using beta-blockers (data not shown). Finally, the present study was correlational, therefore it is not possible to determine the causal relation between the different variables.

Conclusions

The present results add to the literature by showing the association between expressive suppression as a maladaptive emotion regulation strategy and depressive symptoms in patients with CHD. More importantly, the present results showed that expressive suppression has a moderating role in the well-known association between depressive symptoms and reduced cardiac vagal control. Greater use of maladaptive emotion regulation strategies based on expressive suppression potentiated the association between the severity of depressive symptoms and reduced cardiac vagal control. The present results highlight the importance of the assessment of emotion regulation strategies in patients with CHD in order to identify individuals with an increased cardiac risk associated with depressive symptoms. Along the same line of reasoning, the inclusion of psychological intervention aimed at targeting emotion regulation in cardiovascular rehabilitation programs may reduce the impact of depression-related risk in patients with CHD undergoing cardiac rehabilitation.

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Authors contributions

EP, SMB, CG, AP and DP conceived and designed the study; FM and AP gathered the data; FM and EP analyzed the data; FM, EP, and SMB wrote the paper, and all authors reviewed and approved the final manuscript.

Supplementary materials

- Supplemental Digital Content 1. Boxplots of heart rate and vagally-mediated heart rate variability.

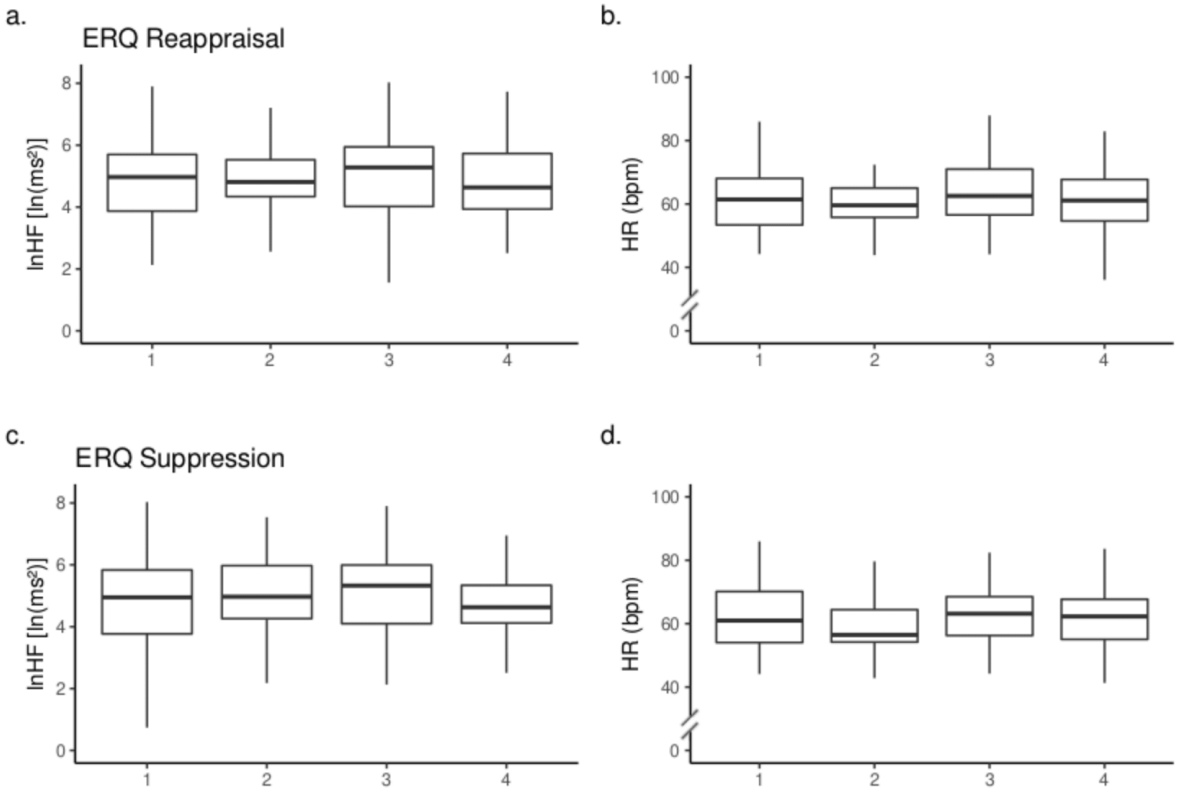

Figure S1: Boxplots of vagally-mediated heart rate variability and heart rate. Within each box, horizontal black lines denote median values; boxes extend from the 25th to the 75th percentile of each group's distribution of values; lower and upper error lines indicate 10th and 90th percentiles, respectively. The sample was divided in four different groups based on a median-split performed on BDI-II and ERQ scores. *Panels a and b.* The figure shows vagally-mediated heart rate variability, as indexed by lnHF, and mean heart rate of the sample divided into four groups. Group 1 includes patients with low BDI-II scores and low ERQ-R scores. Group 2 includes patients with high BDI-II scores and low ERQ-R scores. Group 3 includes patients with low BDI-II scores and high ERQ-R scores. Finally, Group 4 includes patients with both high BDI-II and ERQ-R scores. *Panels c and d.* The figure shows vagally-mediated heart rate variability, as indexed by lnHF, and mean heart rate of the sample divided into four groups. Group 1 includes patients with low scores at the BDI-II and low

scores at the ERQ-S. Group 2 includes patients with high scores at the BDI-II and low scores at the ERQ-S. Group 3 includes patients with low scores at the BDI-II and high scores at the ERQ-S. Ultimately, Group 4 includes patients with high scores both at the BDI-II and the ERQ-S subscale.

Note: lnHF [ln(ms^2)] = Natural logarithm of High Frequency Heart Rate Variability in ms^2; HR (bpm) = Heart Rate (beats per minute).

- Supplemental Digital Content 2. Table showing Pearson's correlations between psychological and physiological measures.

Table S1. Pearson's correlations among physiological and psychological measures.

	HR (bpm)	lnHF [ln(ms^2)]	BDI-II	ERQ-R	ERQ-S
HR (bpm)	-				
lnHF [ln(ms^2)]	-.62 (<.001) ***	-			
BDI-II	.20 (.002) **	-.12 (.061)	-		
ERQ-R	-.06 (.37)	.02 (.74)	.03 (.60)	-	
ERQ-S	-.04 (.53)	.03 (.66)	.16 (.012) *	.16 (.012) *	-

The table shows Pearson's *r* coefficients and *p* values in parentheses.

Note: HR (bpm) = Heart Rate (beats per minute); lnHF [ln(ms^2)] = Natural Logarithm of High Frequency Heart Rate Variability power in ms^2; BDI-II = Beck Depression Inventory II score; ERQ-R = Emotion Regulation Questionnaire - Cognitive Reappraisal score; ERQ-S = Emotion Regulation Questionnaire - Expressive Suppression score.

*** = $p < .001$; ** = $p < .01$; * = $p < .05$