Determinants of Low Anger Control in Patients with Coronary Artery Disease

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ABSTRACT

A low anger control has been associated to coronary artery disease (CAD). However, there is scarce information on predictors of low anger control in those patients. All patients scheduled for elective coronary angiography at a tertiary center for cardiology in South Brazil between 11/30/2009 and 02/03/2010 were considered eligible for inclusion. The inclusion criterion was the presence of significant CAD which was defined as the presence of a stenosis >50% in at least one major epicardial artery. Clinical and sociodemographic characteristics of the patients were registered, and anger aspects were assessed by the Spielberger's Anger Expression Inventory. The anger control score was categorized into quartiles, and the lowest quartil was considered and the first quartile (Low Anger Control) was compared with the others (Proper Anger Control). The medians were compared by the POISSON regression with adjustment for single and multiple robust variances. Three hundred and six patients with 60 ± 9 years old with angiographically proven CAD were included in this study. Our results showed that the younger, diabetic and patients with a family history of CAD presented lower medians for the anger control. Body Mass Index was also correlated with anger control. In the multivariate analysis, however, only family history for coronary artery disease was an independent risk factor for a low anger control. These results provide a better understanding of the relationship between anger control and CAD, and should help to consolidate the knowledge in this field and also help to plan further studies to investigate a cause-effect relationship.
Key words: anger, personality, social determinants of health, coronary artery disease, catheterization, risk factor.

Novelty and Significance

What is already known about the topic?

- Anger appears commonly in psychological stressful situations producing increases in serum cortisol and adrenalin.
- Physiologic and metabolic consequences of this reaction could contribute to the atherogenic process.
- Anger have been linked with a higher risk of coronary artery disease and worst outcomes after a prior event.

What this paper adds?

- A study of factors associated with low anger control in a population of patients with coronary artery disease.
- Results showed that family history of coronary artery disease was an independent predictor of low anger control.
- This knowledge can help clinicians guide their patients to treatments to better management this emotion.

Anger is an emotion that appears commonly in psychological stressful situations producing increases in serum cortisol and adrenalin (Williams, Couper, Din-Dzietham, Nieto, & Folsom, 2007). It has been demonstrated that physiologic and metabolic

consequences of this reaction could contribute to the atherogenic process (Staicu & Cutov, 2010). Anger has been linked to coronary artery disease (CAD), cardiovascular mortality, (Denollet, Gidron, Vrinst, & Conraads, 2010) unhealthy behaviors, smoking and alcohol abuse (Staicu & Cutov, 2010), obesity (Norwood, Bowker, Buchhholz, Henderson, & Flament, 2011) and type 2 diabetes (Tsenkova, Carr, Coe, & Ryff, 2012).

The association between anger and CAD was first demonstrated in a meta-analysis performed by Chida and Steptoe (2009) and since then several dimensions of anger were assessed separately (Sahoo, Padhy, Padhee, Singla, & Sarkar, 2018), as trait anger (Brummett, Boyle, Ortel, Becker, Siegler, & Williams, 2010) or the expression of anger, especially anger-in and anger-out (Davidson & Mostotsky, 2010; László, Jansky, & Ahnve, 2010). Anyway, the association between anger and risk of cardiovascular events has been enough study in large coorte studies as led by interheart researchers (Smyth, O'Donnell, Lamelas, Teo, Rangarajan, & Yusuf, 2016).

The impact of these different dimensions of anger on the occurrence of cardiovascular events was investigated in a prospective cohort study of nearly eight thousand individuals, and only anger control was predictive of an adverse outcome (Haukkala, Konttinen, Loatikainen, Kawachi, & Uutela, 2010). We have also previously demonstrated that lower anger control is an independent predictor of cardiovascular events in patients with CAD (Schmidt, Lopes, Newby, Moura, Stochero, Gottschall, & Quadros, 2013). However, as far as we know, factors associated to a low anger control were not previously investigated in a population of patients with angiographically proven CAD, and this is the objective of the present study.

Method

Participants

This was a prospective cohort study, and all patients scheduled for elective coronary angiography at tertiary center for cardiology in South Brazil, between 11/30/2009 and 02/03/2010 were considered eligible for inclusion. The inclusion criterion was the presence of significant CAD. Exclusion criteria were scheduled for elective percutaneous coronary intervention, valvuloplasty, aortography or vascular angiography. Prior diagnosis of valvular disease, congenital disease or dilated cardiomyopathy with ejection fraction ≤30%. In addition, patients with some cognitive impairment were excluded. All patients were interviewed on the day of the procedure and provided written informed consent.

The study was approved by the institutional review board of the Institute of Cardiology and follows the Declaration of Helsinki. The authors are solely responsible for the design and conduct of the study, all study analyses, the drafting and editing of the paper, and approval of its final contents. No extramural funding was used to support this study.

Procedure

Clinical and socio-economic characteristics, risk factors for CAD, previous medical history, clinical presentation of CAD and history of psychological diagnosis were assessed and included in a dedicated database. The classification of the race was based on the self-declaration of the participants, as well as the presence or absence of the risk factors. Hypertension was defined by previous diagnosis or use of antihypertensive

drugs. Dyslipidemia was considered present in those with previous diagnosis or use of lipid-lowering drugs. Diabetes Mellitus was defined by previous use of insulin or hypoglycemic drugs, or documented fasting glucose >126 mg/dl on two occasions. Depression was defined as the occurrence of at least one episode major of depressive symptoms requiring farmacological treatment. Sedentary lifestyle was assessed by the absence of regular physical activity. For obesity we consider a BMI (Body Mass Index) equal to or greater than 30 kg/m². Family history of CAD was considered present if first degree relatives had AMI or sudden cardiovascular death before age 55 for males and 65 for women.

Coronary angiography procedures were performed either by the femoral or radial approach. All angiographic analyses were performed in at least two views and severity of coronary obstructive lesions was assessed with a previously validated digital caliper system (Siemens Axiom Artis, Munich, Germany). Intracoronary nitroglycerin was routinely given at a dose of 100-200 μg before measurements. Significant CAD was defined as the presence of a stenosis >50% in at least one major epicardial artery.

Anger Assessment

Anger was assessed by the *Spielberger State-Trait Anger Expression Inventory* (STAXI, Spielberger & Biaggio, 2003), on the same day of angiography and score was determined by a psychologist. The STAXI evaluates different aspects of anger, both its intensity and the way it is expressed. It´s divided in eight subscales of anger's assessment: state, trait, temperament, reaction, expression, anger-in, anger out and anger control. The state of anger consists of ten questions with a total score ranging from 10 to 40 points. This scale measures the intensity of the anger at the time of the test, so it was not used in this study. Anger's trait demonstrates enduring trends of personality. It is also evaluated by ten questions with score ranging from 10 to 40 points. The trait of anger is divided in temperament and reaction. The first concerns the intensity of anger in the absence of external stimuli, and the reaction comes as response to external situations. Both are evaluated by four questions with score ranging from 4 to 16 points. The total score of anger trait ranges from 10 to 40 points. As Spielberger and Biaggio (2003) explained the expression of anger provides an assessment of how anger is experienced: suppressed, expressed or controlled. Expression of anger has three subscales: 1) anger-in, when angry feelings are repressed or stored; 2) anger-out, when the individual expresses anger against other people or objects in the environment; and 3) anger control that measures how much the individual tries to control his anger. Each of these subscales is assessed by eight questions, with scores ranging from 8 to 32 points. The total score of anger expression is assessed by the results: total in + total out - control +16.

In a previously study (Schmidt et alia, 2013) we had demonstrated that only anger control was associated with angiographically proven CAD. Therefore, in the present study, we emphasized the analysis of the risk factors associated with the lower anger control.

Data Analyses

The anger control score was divided into quartiles and the first quartile (Low Anger Control) was compared with the others (Proper Angel Control). The correlations between anger control scores and continuous variables were assessed by Spermann coefficients. The medians were compared by the POISSON regression with adjustment for single and multiple robust variances. Included in the multiple analysis variables

with p <0.10. Multicollinearity was tested with the Variance Inflation Factor (VIF) statistic. Considering the cut-off point for 2 points for its determination. A p <.05 was considered statistically significant. All data were analyzed with SPSS 24.0 for Windows statistical package.

Results

During the study period, 1127 patients were scheduled for catheterization, and Figure 1 shows the study flowchart and the main exclusions from this initial patient population. Of the 682 eligible patients, 217 patients did not have CAD, 96 were unable to be interviewed due to medical or cognitive conditions, 33 patients did not consent to participate and 30 patients had other significant cardiology conditions besides CAD. The final sample of the patients was comprised of 306 individuals.
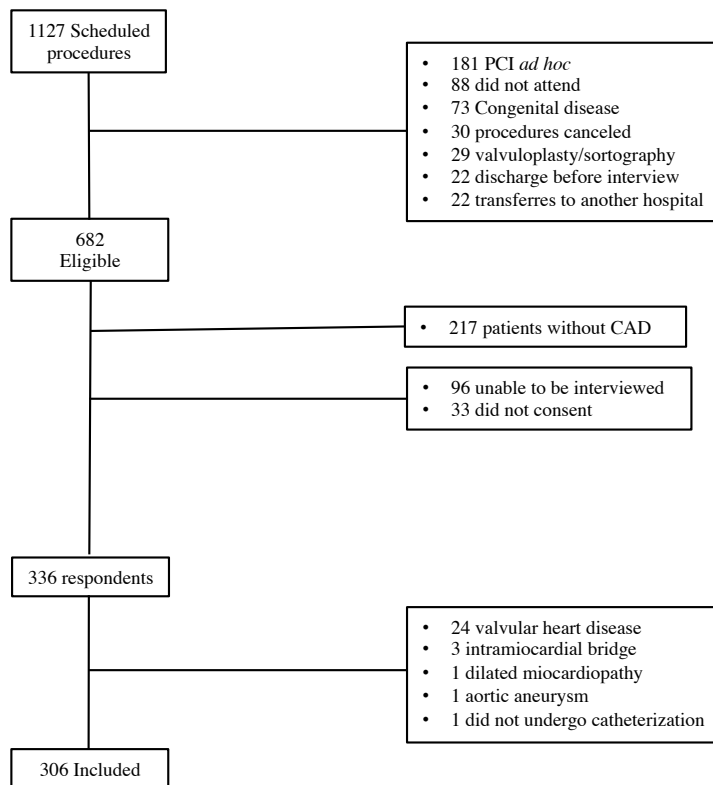
Figure 1. Study flowchart.

135 patients (44% of the cases) had uniarterial lesions; 78 (25%) biarterial lesions; 81 (26%) were triarterial; and 12 (4%) presented lesions in the left main coronary artery. Besides that, 246 (81%) presented severe stenosis and 60 (19%) moderate stenosis. The mean ejection fraction was 63 ± 13%. Table 1 shows the baseline characteristics of the patients according to the medians of low or proper anger control. It was observed that the younger, diabetic and patients with a family history of CAD presented lower

medians for the anger control. BMI was also correlated with anger control. Other risk factors, medical history, length of education and prior diagnosis of depression were not associated with low anger control.

Table 1. Low anger control according to baseline characteristics.

Characteristics	Low Anger Control n (%)	Proper Anger control n (%)	p
Gender Male	38 (44%)	76 (34%)	.14
Afro-descendant	14 (16%)	22 (10%)	.10
Married	50 (58%)	130 (59%)	.97
Employed	30 (35%)	79 (36%)	.96
Living alone	25 (29%)	43 (19%)	.06
Depression,	26 (30%)	55 (25%)	.34
Previous AMI	23 (28%)	73 (33%)	.28
Previous CABG	6 (7.0%)	18 (8.2%)	.73
Previous PCI	14 (16%)	46 (21%)	.37
Diabetes Mellitus	34 (39%)	62 (28%)	.05
Hypertension	72 (84%)	186 (84%)	.86
Smoking	20 (23%)	50 (23%)	.92
Dyslipidemia	45 (52%)	140 (63%)	.07
Sedentary	61 (71%)	157 (66%)	.94
Obesity	40 (46%)	84 (38%)	.180
Family history of CAD	44 (51%)	60 (27%)	<.001
Age, years	(58 ± 9)	(62 ± 10)	.004
Length of education, years	7 ± 6	7 ± 5	.81
BMI, kg/m^2	29 ± 5	28 ± 4	.04

Notes: AMI= Acute Myocardial Infarction; CABG= Coronary Artery Bypass Grafting; PCI= Percutaneous Coronary Intervention; CAD= Coronary Artery Disease, BMI= Body Mass Index.

Table 2 presents correlations among clinical characteristics, different aspects of anger and anger control. Trait: $r=$ -0.37, p <.001, Temperament: $r=$ -0.39, p <.001, Reaction: $r=$ -0.18, p <.001, Anger-in: $r=$ -0.12, p <.05, Anger-out: $r=$ -0.41, p <.001, Anger-expression: $r=$ -67, p <.001) and age ($r=$ 0.19 p <.001) were correlated with anger control, while length of education ($r=$ -0.02; $p=$ .97) and BMI ($r=$ -0.67; $p=$ .24) were not. All subscales had a significant inverse relationship with the anger control. So, the higher trait of anger, anger-out, anger-in and anger expression, less anger control. Age had a positive relationship with anger control, so the older had a better control of this emotion. Anger-out had a positive correlation with BMI ($r=$ 0.14 p <.05).

Table 2. Correlations with anger control (Statistical significance is based on Spermann coefficients).

	A	BMI	LE	AE	At	AT	Ar	AI	AO	AC
Age (A)	--	-.201**	-.209**	-.238**	-.133**	-.128**	-.074	-.113*	-.234**	.196**
BMI	-.201**	--	.026	.028	.085	.073	.098	-.110	.142*	-.067
Length of Education (LE)	-.209**	.026	--	.038	-.094	-.124*	-.030	-.035	.109	-.002
Anger expression (AE)	-.238**	.028	.038	--	.651**	.553**	.457**	.673**	.732**	-.675**
Anger-trait (At)	-.133**	.085	-.094	.651**	--	.852**	.802**	.375**	.614**	-.377**
Anger Temperament (AT)	-.128**	.073	-.124*	.553**	.852**	--	.441**	.267**	.524**	-.393**
Anger reaction (Ar)	-.074	.098	-.030	.457**	.802**	.441**	--	.339**	.394**	-.183**
Anger-In (AI)	-.113*	-.110	-.035	.673**	.375**	.267**	.339**	--	.222**	-.118*
Anger-Out (AO)	-.234**	.142**	.109	.732**	.614**	.524**	.394**	.222**	--	-.421**
Anger-Control (AC)	.196**	-.067	-.002	-.675**	-.377**	-.393**	-.188**	-.118*	-.421**	--

Notes: *= p <.05; **= p <.001.

In the multivariate analysis (Table 3), patients with a family history of coronary artery disease were 87% more risk to has a low anger control. [*Exponentiation of the B coeficiente*= 1.87, p <.001.] Living alone, diabetes, dyslipidemia, BMI and age were not independent risk factors for a low anger control in this multivariate analysis.

Table 3. Poisson Regression with anger control scores as dependent variable.

Characteristics	Exp (B)	95% Wald confidence interval	p
Age	.98	.97-1.00	.10
Family history of CAD	1.87	1.30-2.68	<.001
Living alone	1.31	0.90-1.92	.16
Diabetes	1.27	0.87-1.85	.22
Dyslipidemia	0.72	0.51-1.02	.07
BMI	1.02	0.98-1.07	.25

Notes: CAD= Coronary artery disease; BMI= Body mass index; Exp (B)= Exponentiation of the B coefficient; *p*= based on Poisson Regression.

Discussion

In this study we have analyzed aspects associated with anger control in patients with angiographically proven coronary artery disease (CAD). Our results showed that the younger, diabetic and patients with a family history of CAD presented lower medians for the anger control. BMI was also associated with anger control. In the multivariate analysis, however, only patients with a family history for coronary artery disease were 87% more risk to has a low anger control.

In a large population study conducted in Sweden with 46.393 healthy men, followed for 35 years, the authors reported that poor emotional control was associated with smoking, anxiety, depression and lower schooling. It is interesting to note that these authors reported that family history of CAD were more frequent in men with poor emotional control (Potijk, Janszky, Reijneveld, & Falkstedt, 2016) findings similar to the present paper. The role of heredity was also demonstrated in a study of African-americans in which the children of hypertensive parents had higher systolic and diastolic blood pressure and significantly higher scores on the stroke/temperament and rage scores (Johnson, 1989) than children of normotensive individuals. The authors thus demonstrated the association between cardiovascular reactivity, emotional factors and parental history. The same pattern appears to occur in the case of a history of CAD. Higher scores of anger consequently lead to less control and could trigger a chronic inflammatory process. These studies suggest that there is an inherited pattern of temperament, of reactivity to the situations experienced, which makes up the personality. The personality includes how the individual responds cognitively, emotionally and physiologically to the environment.

Besides the mechanisms by which low anger control was associated with CAD and others predictors were not specifically addressed in our study, we know that the anger's source is the amygdala, which upon perception of danger prepares the body for "fight or flight". (McCorry, 2007). This response triggers a series of hormonal changes, especially an excessive increase in circulating catecholamines and corticosteroids, which precipitates a higher demand for oxygen and potentially, myocardial ischemia. So, subjects with lower anger control trigger more frequently adverse physiological responses to day by day life events. The catecholamine's and cortisol's excess lead to exacerbation of endothelial dysfunction and coronary atherosclerosis, increasing the risk of cardiovascular events (Bacon, Ring, & Hee, 2006).

As a result, there are increases in the blood pressure, and in the inotropism and chronotropism of the heart, which precipitates a higher demand for oxygen and myocardial ischemia. The corticosteroids increase protein breakdown to be transformed into glucose by the liver, and this increased blood glucose can be used by tissues in the

production of energy, which leads to an increase in blood glucose. (Cohen, Panguluri, Na, & Whooley, 2010). Probably for this reason, the relationship between glucose metabolism and anger has also been investigated. As well as we found association of low control with diabetes, Tsenkova, Carr, Coe, and Ryff (2012) found the low anger control was associated with high glucose and conclude that anger as a potential risk factor for type 2 diabetes and its control is related to glycemic control.

In the same way, anger was a BMI predictor in patients with metabolic syndrome (García Silva, Navarrete, Rodríguez, Peralta Ramírez, García, & Caballo, 2018) and previous study with adolescents (Albayrak & Kutlu, 2012) found a positive correlation with anger control and BMI. These results corroborate our findings although no statistical significance has been found.

Some studies suggest that inflammatory proteins troponina, interleukin (Demarble, Morkowitz, Tardif, & D'Antono, 2014) C-reactive protein (Gross, Groer, & Thomas, 2014) and endothelin (Burg, Soufer, Lampert, Collins, & Soufer, 2014), highly vulnerable to psychological and behavioral factors, could be one of the mechanisms by which hostility and anger (Demarble et aliaia, 2014), or even low anger control, are contributing to cardiovascular risk. In this association line between anger and biological factors, Denson, Dobson-Stone, Ronay, Von Hippel, & Schira (2014) correlated aggressiveness with a polymorphism of monoamine oxidase-A gene. They suggest that men with low-expression allelle showed increased amygdala activation after insult experiment, but men with high-expression allelle did not.

It was reported in one study that aggressiveness was 11% higher in women taking cholesterol-lowering medications compared to those who did not take it (Olson, Kelsey, Matthews, Merz, Eteiba, McGorray, Cornell, Vido, & Muldoon, 2008) This may be the reason why dyslipidemia appears associated with low anger control.

Regarding the other factors, we found that age presented a significant correlation with anger control scale, and we observe that the younger shows lower anger control than others. It can be hypothesized that with the aging process may favour the development of new strategies to deal with emotions and thoughts, but in our patient population age was not an independent predictor of low anger control. Studies showed that educational and cognitive strategies (Prochaska, 2008; Bahremand, Alikhani, Zakiei, Janjani, & Aghaei, 2015) seem effective in reducing negative emotions and developing positive strategies, however, more studies to evaluate its effectiveness are required.

Our results showed that anger control was inversely correlated with another anger scales, corroborating Bresin & Robinson (2013) study. In addition to a pattern of inherited temperament, interpretations of events seem to be fundamental for the triggering of physiological responses. The way people interpret life events can influence how they relate to others and how they respond emotionally to a specific interaction. These individual interpretations go through an affective-cognitive process of understanding the world that reflects one's own way of being. Thus, due to the inherent difficulties of relationships, the presence of a companion could exacerbate feelings of anger, diminishing their control, since they are inversely proportional. It can be assumed that "living alone" is used as an avoidance strategy by patients with less control of anger, producing some comfort in minimizing stressful situations. In this way, social self-exclusion could reduce aggression against others and increase pro-social and relieving behavior (Twenge, Baumeister, Tice, Stucke, 2001). This strategy has already been described in patients with Type-D personality (Van den Broek, Martens, Nyklícek, Van der Voort, Pedersen, 2007). Still in relation to isolation, Cacioppo and Hawkley (2009)

have already described that the brains of lonely people are on high alert for social threats, so they tend to view their social world as threatening and punitive. When other people's behaviors validate negative social expectations, they are reinforced and that increases the likelihood of the individual to behave in a way that alienates others. Consequently, solitary individuals may perceive themselves as passive victims in their social world, but are active contributors through their self-protective and paradoxically self-destructive interactions with other people.

This study evaluated patients scheduled for elective coronary angiography in an approximately 3-month period in a tertiary cardiology center. These results may not apply to a lower risk population or to those presenting acute coronary syndromes. Hypertension, dyslipidemia, and diabetes mellitus were defined by previous diagnosis and use of drugs to treat these conditions, but the study protocol did not include assessment of blood pressure levels and laboratory evaluation in each patient. Likewise, the BMI was calculated based on weight and height referred by the participants, but none of these measurements was performed. We did not evaluate adherence to medications, which could be a confounder, related to both the occurrence of events and self regulation. Additionally, we identified variables associated with low anger control among patients with CAD, an important aspect that has been scarcely assessed. Taken together, our results and those from other studies suggest that anger control may be a suitable target for psychological interventions aimed at reducing cardiovascular events among patients with or at risk for CAD. The investigation of factors associated with lower anger control is also important when considering the design of a randomized clinical trial to assess the effect of anger management on cardiovascular outcomes, which would be the next logical step in this line of investigation.

In patients with angiographically proven CAD, age, BMI, living alone, dyslipidemia, diabetes and family history of CAD were associated with low anger control, however, only the family history of CAD was an independent predictor for low control. These results provide a better understanding of the relationship between anger control and CAD, and should help to consolidate the knowledge in this field and also help to plan further studies to investigate a cause-effect relationship. This knowledge can also help clinicians guide their patients to supplemental treatments to better management this emotion.

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