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Exploring the role of adult attachment, major depression and childhood trauma in arterial stiffness: A preliminary study☆

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ABSTRACT

Objective: Prior research indicates a noteworthy and intricate connection between depression and subclinical atherosclerosis. Nevertheless, the biological and psychological mechanisms that underlie this association are not yet fully understood. To address this gap, this exploratory study aimed to examine the relationship between active clinical depression and arterial stiffness (AS), with a particular focus on the potential mediating roles of attachment security and childhood trauma.

Methods: In this cross-sectional study, we examined 38 patients with active major depression free of dyslipidemia, diabetes mellitus, hypertension, and obesity and 32 healthy controls. All participants underwent blood tests, psychometric assessments, and AS measurements using the Mobil-O-Graph arteriograph system. AS severity was evaluated using an augmentation index (AIx) normalized to 75 beats/min.

Results: In the absence of defined clinical cardiovascular risk factors, there was no significant difference in AIx between individuals with depression and healthy controls ($p = .75$). Patients with longer intervals between depressive episodes had lower AIx ($r = -0.44$, $p < .01$). Insecure attachment and childhood trauma did not significantly associate with AIx in patients. Whereas insecure attachment was positively correlated with AIx only in healthy controls ($r = 0.50$, $p = 01$).

Conclusions: Our analysis of established risk factors for atherosclerosis revealed that depression and childhood trauma had no significant relationship with AS. However, we did identify a novel finding: insecure attachment was significantly associated with AS severity in healthy adults without defined cardiovascular risk factors for the first time. To our knowledge, this is the first study to demonstrate this relationship.

1. Introduction

Cardiovascular diseases (CVD) are a severe cause of morbidity and mortality and are responsible for many deaths worldwide today [1]. Arterial stiffness (AS), which describes the rigidity of the arterial wall and the capability of an artery to expand and contract in response to pressure changes, is among the primary processes leading to CVD. The measurement of AS detects the earliest signs of structural and functional changes in the vessel wall and is accepted to be a significant predictor of CVD [2,3] and has been widely used as one of the indicators for studies investigating subclinical atherosclerosis. Research has revealed that besides traditional cardiovascular risk factors [2], psychological adversities also play a significant role in developing AS through inflammation, endothelial dysfunction, dysregulation of the autonomic nervous system (ANS), and unhealthy behavioral patterns [1,4–6].

A significant number of studies has drawn attention to the complex association between depressive symptoms and CVD by showing that depression can occur both as a cause and a consequence of CVD and can

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even increase mortality due to CVD [7–13]. Studies investigating the relationship between AS and depression are large sample-sized population-based studies, but most studies use self-reported scales to identify individuals with depression [3,6,14–16]. In addition, only a few studies examine AS in populations whose diagnosis of current clinical depression has been confirmed by psychiatric interviews [17–19]. When the results of all these studies are taken together, although there are inconsistent results, a considerable number of studies showed the AS increase in depression and emphasized the importance of recognizing the concomitant factors that play a role in it.

Studies have revealed that, apart from increased sedentary life and unhealthy diet, the presence of depression alone can cause AS through endothelial dysfunction. Also, researchers point out that chronic low-grade inflammation, another mechanism that plays a role in the development of depression and AS, can occur very early due to psychosocial stressors [20,21]. These findings paved the way for research investigating the relationship between childhood stress and AS. In addition to negative studies [3,18], several studies revealed that adverse childhood experiences and exposure to childhood trauma are related to increased AS in both pediatric and adult populations [22,23].

Attachment, considered one of the determinants of life-long stress starting from childhood, refers to an individual's emotional bonding pattern in interpersonal relationships. It is thought that this pattern, which is accepted to be shaped by the attitude of the mother or primary caregiver to the individual during infancy, is manifested in the person's later relationships and determines the emotional well-being and physiological stress response that the person experiences in a social interaction throughout life [24]. In the absence of a reliable and sensitive approach at an early age, the child cannot develop an inner sense of security and trust in others, resulting in ambivalent or avoidant insecure attachment patterns. Adults with insecure attachment styles may mistrust others and have difficulty forming or utilizing supportive social relationships; therefore, they may be more prone to chronic stress in various social relationships [25,26]. The presence of an insecure attachment pattern has been considered a significant risk factor for depression and anxiety disorders [27]. In addition, animal and human studies revealed that insecure attachment, along with childhood adversities, can affect physical health through several biological mechanisms and unhealthy lifestyle behaviors [28,29]. Individuals who have insecure attachment patterns display disrupted inflammatory responses [29], overactive cortisol abnormalities [30,31], and higher systolic and diastolic blood pressure in specific social interactions [26]. Vagal tone, which provides regulation of excitation by limiting heart rate increase, was also found to be lower in individuals with insecure attachment patterns [28].

On the other hand, very recent studies show that the oxytocin hormone, a biological substrate of human attachment which has a central role in the formation of emotional bonds across the lifespan, may constitute an essential target for the prevention and possibly treatment of cardiovascular diseases [32,33]. Despite a growing body of evidence showing the relationship between attachment style and physical health, only one adolescent study investigates the impact of attachment style on AS [34]. To the best of our knowledge, no study investigated the relationship between attachment patterns and AS in adults.

Considering the findings mentioned above, this study aimed to determine the interrelation between depression variables and AS and elucidate the relationship between attachment patterns and AS in clinically depressed patients and healthy adults. As the available evidence from previous studies on the role and direction of predictive and determinant psychological factors in the relationship between depression and AS is mostly heterogeneous, we did not put forward specific hypotheses and followed an exploratory approach.

2. Methods

2.1. Sample and study procedure

We conducted this cross-sectional study on patients who were followed up with a diagnosis of major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition criteria (DSM 5, APA 2013) at Marmara University Hospital's psychiatry outpatient clinic in Istanbul, Turkey. After routine examination, patients who gave written informed consent to participate were referred to the research psychiatrist for blood tests and evaluation for eligibility. Patients were not included in the assessment if they met one of the following criteria: (1) age < 18 years and > 65 years, (2) illiteracy, (3) body mass index (BMI) ≥ 30, (4) a history of diabetes mellitus, hyperlipidemia, hypertension (HT) or known decompensated (serious) medical illness, (5) usage of antihypertensive, antidiabetic or lipid-lowering medication, (6) history of nicotine, alcohol, or substance addiction or current regular usage of them, or, (7) having any axis I psychiatric disorder comorbidity. After the first evaluation, researchers subject participants to blood tests and cardiac examinations. In addition, patients were excluded from the study if one of the following tests revealed any abnormality: fasting plasma glucose levels of >126 mg/ dL in ≥3 measurements, total serum cholesterol ≥200 mg/dl, serum triglyceride ≥150 mg/dl, low-density lipoprotein cholesterol ≥130 mg/dl or systolic and/or diastolic blood pressure ≥ 140/90 mmHg. We recruited healthy controls from a participant pool composed of hospital staff and medical school who volunteered for empirical studies in the hospital to earn brief psychological counseling. We phoned and invited those not diagnosed with any mental illness before and who did not work in any psychiatry-related departments (to remove potential coercion or any conflict of interest). We interviewed those who accepted to participate as a volunteer. The majority of healthy participants represented non-medical jobs, such as cleaning ($n = 10$, 31%) and administration operations (i.e., business office, clerical support, medical coding, security staff; $n = 11$, 34%), and others were nurses ($n = 6$, 19%) and interns ($n = 5$, 16%). Our clinical interviews suggested that none were eligible for any psychiatric diagnosis. Persons who did not meet any of the above-mentioned exclusion criteria, numbered 1 to 7, were subjected to the same cardiac examinations and blood tests. Following evaluation, individuals who met the inclusion criteria were included in AS measurement. Most of the participants eligible for the study underwent AS measurement on the same day with psychometric assessment; two participants were assessed on the following 5th and 7th day of the psychometric evaluation (mean = 1, SD = 0.25 days).

The study was carried out by the values outlined in the Helsinki Declaration Criteria and approved by the Local Ethics Committee of Marmara University (approval number: 09.2017.431).

2.2. Data acquisition

2.2.1. Psychometric measures

2.2.1.1. Assessment of clinical depression and trait anxiety. After a qualified psychiatrist diagnosed the patients with major depression, the research psychiatrist applied the Structured Clinical Interview for DSM (SCID) to exclude comorbid diagnoses. Information about the history of depression, its clinical characteristics, and other coronary health indicators was obtained in another interview with a semi-structured data form developed by the research team. We present the details of patients' depression characteristics in Table 3. We used the Beck Depression Inventory (BDI), a 21-item self-report scale, to assess the severity and the constituents of depressive symptoms [35,36]. To evaluate the potential confounding effect of chronic subclinical anxiety, we also used the "Trait Anxiety Subscale" of the Spielberger State-Trait Anxiety Inventory (STAI), which provides a reliable measure of trait anxiety with 20 items

[37,38].

2.2.1.2. Assessment of attachment styles. We used the Adult Attachment Scale (AAS) to measure the participants' attachment styles. This self-report scale evaluates secure and insecure (anxious-avoidant and anxious-ambivalent) adult attachment styles. The Turkish version includes six statements for each attachment pattern (i.e., secure, avoidant, ambivalent). Respondents rate these sentences on a 4-point Likert-type scale according to the suitability of items for the respondents' relationships with significant others. Each subject gets three attachment scores corresponding to the three styles [39,40].

2.2.1.3. Assessment of childhood trauma. We used the Turkish version of the Childhood Trauma Questionnaire (CTQ) to evaluate adverse experiences in childhood. The scale comprises 28 questions rated in a 5-point Likert-type format. Five types of maltreatment -sexual, physical, emotional abuse, and emotional and physical neglect- are evaluated retrospectively and quantitatively [41,42]. The cut-off score based on the findings of the studies was accepted as 35 for the Turkish population. This limit is assumed to be 5 for physical and sexual abuse, 7 for emotional abuse and physical neglect, and 12 for emotional neglect [42].

2.2.1.4. Assessment of arterial stiffness parameters. We assessed augmentation index (AIx) (%) and pulse wave velocity (PWV) (m/s) parameters as a measure of AS. The measurement was conducted with a Mobil-O-Graph arteriograph system (IEM GmbH, Stolberg, Germany) [43]. Measurements were done by one technician, who was blind to the participants' diagnosis. The technician performed AS measurements with the subjects in the supine position in a quiet, temperature-controlled room (22–24 °C) early morning. Participants had refrained from eating or drinking alcohol, coffee, or tea for the last 12 h. The arteriograph system detects signals from the brachial artery with cuff pressure up to 35 mmHg higher than systolic pressure. This technique's basis is the myocardium's contraction generating a pulse wave (early systolic peak) that travels down the aorta. The wave is reflected from the aortic wall at the distal branching point, generating a second reflected wave (late systolic peak), the morphology of which depends upon the stiffness of the large artery. PWV and AIx, adjusted for a heart rate of 75 bpm, were recalculated according to current guidelines, using the amplitude and time difference of the first and second waves [44]. At least two consecutive measurements will be done mean of the indices would be recorded. If indices vary >5%, a third measurement would be done and mean of the nearest two measurements would be collected.

2.3. Data analyses

All statistical analyses were conducted using SPSS Version 20. We performed descriptive statistics on sociodemographic variables, physical health indicators of all participants as well as depression characteristics of the patient group. To test interrelations among depression variables, attachment patterns, and AS in clinically depressed patients and healthy adults; and to examine correlations among psychological measures, characteristics of depression history of patients, and cardiovascular indicators for the patient group, we conducted Pearson Correlation Coefficient Analysis. Independent sample *t*-tests and Chi-square tests were utilized for group comparisons. For all analyses, the statistical significance was defined as $p < .05$.

3. Results

We demonstrate the sociodemographic characteristics of patients and healthy controls in Table 1. Patients and healthy controls did not significantly differ on sociodemographic characteristics, except employment status. There was significantly more unemployed in the patient group ($n = 28, 74\%$) compared to the control group ($n = 4, 13\%$), $\chi^2 (1) = 35.03$, $p < .001$.

Table 2 presents the health characteristics of patients and healthy groups. Group comparisons revealed no statistically significant group difference in coronary health indicators of patients and healthy controls except triglyceride level (mg/dl) and the presence of any physical illness, which are both higher for the patient group.

Table 3 illustrates the depression characteristics of patients. None of

Table 1
Sociodemographic characteristics of patients and healthy controls.

	Patient group (n = 38)		Healthy group (n = 32)		Difference test
	Mean	Std. Dev.	Mean	Std. Dev.	
Age	37.9	10.3	37.7	10.3	t (68) = 0.06 p = .95
	Frequency	%	Frequency	%	
Gender					
Female	33	87	22	69	χ^2 (1) = 3.38
Male	5	13	10	31	p = .07
Marital status					
Married	30	80	24	75	χ^2 (2) = 5.53
Single	4	10	8	25	p = .06
Other (divorced, widow, etc.)	4	10	0	0	
Education					χ^2 (3) = 3.07
Primary school	17	43	9	28	p = .38
High school	11	27	10	31	
Bachelor degree	9	23	10	31	
Master's degree or more	1	7	3	10	
Employment					**χ^2 (1) = 35.03** $p <$ *.001*
Employed	10	26	28	88	
Unemployed	28	74	4	12	

Table 2
Health indicators of patients and healthy controls.

	Patient group (n = 38)		Healthy group (n = 32)		Difference Test
	Mean	Std. Dev.	Mean	Std. Dev.	t-test df = 68
Height (cm)	161.3	8.1	166.6	10.8	**−2.37 p = .02**
Weight (kg)	66.3	11.8	70.7	13.7	−1.46 p = .15
Body mass index	25.3	4.4	25.5	4.8	−0.17 p = .87
Total cholesterol level (mg/dl)	175.3	19.1	165.1	16.0	1.90 p = .22
Triglyceride (mg/dl)	101.1	25.9	74.2	32.3	**3.48 p < .001**
HDL (mg/dl)	54.5	13.2	50.8	12.8	1.19 p = .28
LDL (mg/dl)	105.3	17.1	99.3	16.2	1.22 p = .24
Systolic pressure (mmHg)	118.2	10.6	121.8	20.0	−0.95 p = .34
Diastolic pressure (mmHg)	76.1	10.9	75.1	16.1	0.33 p = .74
	Frequency	%	Frequency	%	
Level of physical activity					χ^2 (3) = 4.59 p = .21
No	34	90	26	82	
Less than one hour per week	2	6	0	0	
1–3 h per week	1	2	3	9	
>3 h per week	1	2	3	9	
Family history of coronary disease					χ^2 (1) = 1.10 p = .29
Yes	19	50	12	38	
No	19	50	20	62	
Presence of physical illness					**χ^2 (1) = 6.32 p = .01**
Yes	18	47	6	19	
No	20	53	26	81	

Table 3
Depression characteristics of patients ($n = 38$).

	Mean	Std. Dev.
Total number of depressive episodes	1.9	1.1
The onset of age for depression diagnosis	30.4	11.2
Duration of the latest depressive episode (week)	88.1	129.2
Duration of remission among depressive episodes (year)	1.9	0.8
	Frequency	%
History of hospitalization due to depression		
Yes	3	8
No	35	92
Number of hospitalization due to a depression attack		
0	35	94
1	1	2
2	1	2
3	1	2
History of Electroconvulsive Therapy		
Yes	0	0
No	38	100
Family history of psychiatric illness		
Yes	16	42
No	22	58
Number of suicide attempts		
0	30	80
1	4	10
2	4	10
Family history of suicide attempts		
Yes	7	18
No	31	82
Current usage of anti-depressive medication		
Yes	32	84
No	6	16

the patients had a history of electroconvulsive therapy. Most patients did not have a history of hospitalization due to depression ($n = 35$, 92%), suicide attempts ($n = 30$, 79%), or a family history of suicide attempts ($n = 31$, 82%). Nearly half reported a family history of psychiatric illness ($n = 22$, 58%). Most of the patient group was under antidepressant treatment at the time of inclusion in the study ($n = 32$, 84%).

Table 4 compares the psychological characteristics of patients and healthy controls. Independent sample *t*-tests revealed that patients (mean = 44.5, SD = 15.6) reported significantly higher levels of childhood trauma experiences than healthy participants (mean = 31.8, SD = 9.7, $t\,(68) = 3.99$, $p < .001$).

As expected, patients (mean = 24.1, SD = 11.8) reported higher depression than healthy controls (mean = 4.4, SD = 4.6, $t\,(68) = 8.81$, $p < .001$). They similarly reported significantly higher levels of trait anxiety (mean = 54.8, SD = 10.4) compared to healthy participants (mean = 39.5, SD = 7.9, $t(68) = 6.79$, $p < .001$). Patients also reported a significantly higher frequency of insecure attachment than controls ($\chi^2\,(1) = 11.28$, $p = .001$). In terms of the indicators of AS, patients and healthy controls did not significantly differ on AIx ($t\,(68) = 0.31$, $p = .76$) or PWV ($t\,(68) = -0.08$, $p = .94$).

Table 4
Comparison of patients and healthy controls on trauma, childhood abuse, anxiety level, depression, and adult attachment.

	Patient group (n = 38)		Healthy group (n = 32)		Difference test
Psychological variables	Mean	Std. Dev.	Mean	Std. Dev.	t-test, df = 68
CTQ total score	44.5	15.6	31.8	9.7	3.99 $p < .001$
Trait anxiety	54.8	10.4	39.5	7.9	6.79 $p < .001$
BDI score	24.1	11.8	4.4	4.6	8.81 $p < .001$
	Frequency	%	Frequency	%	Chi-square df = 1
Adult attachment, secure	12	32	23	72	11.28 $p = .001$
Adult attachment, insecure	26	68	9	28	
Indices of arterial stiffness	Mean	Std. Dev.	Mean	Std. Dev.	t-test df = 68
Augmentation index (AIx)	24.2	10.7	23.3	12.5	0.31 $p = .76$
Pulse wave velocity (Pwv)	6.1	1.1	6.1	1.2	−0.08 $p = .94$

df = degrees of freedom. CTQ: Childhood trauma questionnaire. BDI: Beck depression inventory.

We presented the correlations between AS indicators, other cardiac health indicators, and psychological measures of patients and healthy controls in Table 5. In terms of depression variables: partial correlation analysis revealed that the duration of the latest depressive episodes (week) had significant positive correlations with triglyceride levels of patients ($r = 0.68$, $p < .001$) and LDL ($r = 0.54$, $p < .001$), controlling for age. The onset of age for depression diagnosis was significantly correlated with lower HDL ($r = -0.36$, $p = .03$), controlling for age. Duration of remission among depressive attacks had a significant negative correlation with AIx ($r = -0.33$, $p = .04$) but a positive significant correlation with diastolic pressure ($r = 0.41$, $p = .02$), all controlling for age.

Regarding the relationship between psychological variables and AS: the scores of CTQ, trait anxiety, and BDI were not significantly correlated with AS indicators in either group. While insecure attachment did not show any relationship with AS indicators in the depression group, there was a significant positive correlation between the insecure attachment and AIx level in healthy participants (r=. 50, $p < .01$).

4. Discussion

In this exploratory study, we examined how the clinical diagnosis of active depression and relevant variables affect the association between depression and AS, especially the role of attachment patterns and childhood trauma in this relationship. The first of the significant findings is that, in the absence of dyslipidemia, diabetes mellitus, hypertension, and obesity, AS was not higher in patients with depression than in healthy controls. Second, patients with higher duration of remission periods between depressive episodes had lower AS. Third, despite the higher severity of insecure attachment and childhood trauma in the patient group, there was no significant relationship between AS and insecure attachment or childhood trauma. Insecure attachment significantly correlated with AS in healthy subjects; even cardiovascular health indicators were within normal limits.

Studies examining the relationship between AS and depression with different AS assessment techniques reveal inconsistent results according to the evidence obtained to date, though evidence indicating that depression increases AS outweighs [6,19]. Although the positive studies had quite large samples, they were conducted in the general population using only self-reported scales without clinical confirmation of current depressive episodes, or they included lifelong depression in addition to active depressive symptoms [3,6,15,16]. For instance, in one study, only 8.8% of the probands were in a current depressive episode during the recruitment [14]. In another, a lifetime history of depression was assessed via verbal interview and linked to a previous hospital-based clinical depression diagnosis, although the current rate of patients with depression is not given [15]. We strongly argue that identifying depressed subjects without clinical examination may lead to an overdiagnosis of depression. For example, psychological stress-related disorders such as adjustment disorder, prolonged grief, or anxiety may be misclassified as depression. In addition, subjects with not a severe systemic disease but subtle medical conditions (anemia, vitamin deficiencies), and individuals with "cytokine-induced sickness behavior," which is defined as physiological and behavioral changes during a nonspecific infection or inflammation, can easily report themselves as depressed due to fatigue, decreased interest in their environment, fatigue, sleep, and appetite changes [45]. In support of our opinion, two studies have shown that AS is related to more affective and vegetative symptoms of depression than cognitive symptoms, emphasizing the role of inflammatory processes [14,46]. Although we did not include people with severe medical conditions in our study, the higher prevalence of

Table 5
Pearson correlation analyses.

Patient group (n = 38)	Augmentation index	Pulse wave velocity	Body mass index	Total cholesterol level	Triglyceride	HDL	LDL	Systolic pressure	Diastolic pressure
CTQ total score	−0.13	−0.18	−0.20	−0.29	−0.19	−0.07	−0.21	−0.16	−0.27
CTQ – emotional abuse	−0.08	−0.10	−0.22	**−0.33**	−0.24	−0.09	−0.23	−0.26	−0.29
CTQ- emotional neglect	0.02	−0.25	−0.02	−0.19	−0.14	−0.06	−0.07	−0.07	−0.19
CTQ – physical abuse	−0.23	−0.14	−0.06	−0.18	−0.14	−0.14	−0.13	−0.20	−0.24
CTQ- physical neglect	−0.04	−0.21	**−0.34**	−0.29	−0.09	−0.04	−0.23	−0.00	−0.06
CTQ – sexual abuse	−0.21	0.01	**−0.40**	−0.16	−0.12	0.11	−0.18	0.05	−0.11
CTQ - minimization	0.29	0.10	0.02	0.07	−0.08	−0.18	0.01	−0.15	0.13
Trait anxiety	0.02	−0.27	−0.05	0.05	0.07	−0.11	0.01	−0.02	0.01
Beck depression score	−0.14	−0.13	−0.11	0.10	0.19	−0.16	0.02	−0.02	0.07
Adult attachment (0 = secure, 1 = insecure)	−0.21	−0.27	0.07	0.01	0.11	−0.03	0.08	−0.17	−0.22
Total number of depressive episodes	.17[a]	-.10[a]	-.08[a]	-.08[a]	-.24[a]	.22[a]	-.03[a]	.06[a]	-.08[a]
The onset of age for depression diagnosis	.01[a]	-.05[a]	.28[a]	-.19[a]	-.02[a]	**-.36[a]**	-.10[a]	-.33[a]	-.14[a]
Duration of the latest depressive episode (week)	-.24[a]	.08[a]	.28[a]	.28[a]	**.68[a]**	-.06[a]	**.54[a]**	.27[a]	.23[a]
Duration of remission among depressive attacks (year)	**-.33[a]**	-.12[a]	.15[a]	-.08[a]	.18[a]	-.25[a]	-.05[a]	.07[a]	**.41[a]**
Anti-depressive medication (1 = no, 0 = yes)	−0.20	0.02	−0.15	−0.08	−0.16	0.13	−0.22	0.11	0.12

Healthy Controls (n = 32)	Augmentation index	Pulse wave velocity	Body mass index	Total cholesterol level	Triglyceride	HDL	LDL	Systolic pressure	Diastolic pressure
CTQ total score	0.02	0.12	0.26	−0.19	0.12	−0.09	−0.27	0.19	0.20
CTQ – emotional abuse	0.04	0.07	0.19	−0.18	0.03	0.09	−0.29	0.17	0.26
CTQ- emotional neglect	−0.04	0.17	0.26	−0.21	0.11	−0.17	−0.24	0.16	0.13
CTQ – physical abuse	−0.03	0.06	0.16	−0.15	0.07	−0.04	−0.21	0.20	0.26
CTQ- physical neglect	0.15	0.10	0.24	−0.01	0.24	−0.22	−0.03	0.06	−0.13
CTQ – sexual abuse	–	–	–	–	–	–	–	–	–
CTQ - minimization	−0.17	−0.19	−0.19	0.03	0.01	0.08	0.01	−0.15	0.05
Trait anxiety	0.11	0.19	0.23	−0.03	−0.08	0.20	−0.08	−0.11	−0.14
Beck depression score	0.12	−0.03	−0.03	0.01	−0.21	0.17	0.03	−0.06	−0.04
Adult attachment (0 = secure, 1 = insecure)	**0.50**	0.12	0.13	−0.01	−0.13	0.24	−0.05	0.18	0.12

Note: The absolute value of correlation coefficients that were equal to or higher than 0.33 were significant at $p < .05$; while those equal to or higher than 0.50 were significant at $p < .01$. CTQ: Childhood trauma questionnaire—[a] Partial correlation coefficient controlling for age. Only one healthy control reported a history of sexual abuse, and therefore, we could not compare the groups on this variable.

physical health comorbidities in the patient group also indicates the importance of clinical diagnosis in clarifying the relationship between AS and depression.

To the extent of our knowledge, there is a limited number of studies assessing AS in clinically diagnosed depression. Consistent with our findings, two found no difference between healthy controls and depression [17,18]. One large sample-sized study found higher levels of AS positively correlated with current depression severity and longer symptom duration [19]. Additionally, researchers reported that subjects with remitted depressive or anxiety disorders did not exhibit increased stiffness. The former results are consistent with our non-significant findings, while the latter contradicts our index results. There may be several reasons for these differences. Firstly, although the authors stated that the results did not change when patients with CVD diagnosis or defined risk factors (HT, DM) were excluded, considering the unhealthy lifestyles and sedentary lives of depressed patients, not performing any blood tests on people with active depression reduces the reliability of the results. For example, the duration of the last depressive episode had a significant positive correlation with triglyceride levels and LDL levels in our sample. Moreover, approximately two months between the AS measurement and the depression assessment will likely affect the results. Finally, another important point is that the use of antidepressants in their patient population is relatively low compared to our patient group [19]. Another plausible explanation of our non-significant finding is that the use of antidepressant medication may have reduced the severity of AS in the patient group. The beneficial effect of antidepressants on AS has been revealed in various clinical and in vitro studies [47–50]. A recent meta-analysis showed that SSRIs significantly improved flow-mediated dilation (FMD), which is the gold-standard method for evaluating artery endothelial function [51]. Although there are inconsistent results among antidepressants, preclinical studies suggest that SSRIs exert their endothelial damage-reducing effect through anti-inflammatory activity on endothelial cells, reducing circulating cytokines, improving platelet function, and modulating vascular tone [48,52]. Investigators also stated that AS reduced more in those who responded better to antidepressants than those who did not [48,49].

Another possible reason for the lack of difference in AS severity between the depression group and healthy controls may be related to the high trait anxiety levels in healthy controls, even if there is no history of psychiatric treatment and no current clinical diagnosis with a clinical interview [53].

This study found no significant relationship between childhood trauma, insecure attachment, and AS severity in patients. In contrast, we detected a positive correlation between insecure attachment and AS in healthy participants. Our findings support studies suggesting that the relationship between childhood traumas and CVD is moderated by the severity of depression and anxiety symptoms [3]. Additionally, when we take all the results together, we suggest that these psychosocial stressors may increase AS in depression mainly through disease-promoting unhealthy behaviors and risk factors. The only study regarding attachment examined the role of social relationships and negative emotional traits in developing central adiposity and AS in healthy adolescents. Researchers

reported that adolescents with greater anxious-insecure attachment and total hostility had greater subsequent AS [34]. Although, this finding is in line with our research finding further replication studies with larger samples are required to understand the relationships between attachment security and AS.

Several limitations should be noted while interpreting the results. First, the critical point is that our findings' external validity is limited due to our relatively small sample size. Our findings may not be generalizable to the broader community of patients with major depression diagnoses. Hence, given the limited power, non-significant results should be approached with caution. The sociodemographic and clinical characteristics of the patient group revealed that it is a young and female-dominated group, clinically not severe, and with good functionality (based on the occupational status). Taking into account gender-specific differences in PWV and AI measurement results in the literature [54], the non-significant gender imbalance between groups may have affected the results. Moreover, considering that smoking, alcohol, and substance use may have confounding effects on the relationship between AS and depression, we did not include patients who have these habits. But not including these patients in our study may have led us to examine a much more resilient sample than the general population of patients with depression. Readers should keep in mind that this sample may not represent major depression patients. We recommend future studies replicate ours in a larger clinical sample to expand their generalization to the depression population. Second, our healthy control group may not be representative of the population. We recruited a sample of hospital staff and included those without a psychiatric diagnosis. Regardless of their line of work, hospital employees could not be typical of the population from which the cases originated. Additionally, it is unclear whether results are specific to depression or a general psychopathology measure when all other psychiatric disorders are excluded; therefore, restricting the study to include healthy controls may have generated a bias. We recommend future studies employ a random sample of individuals from which cases arose and compare patients diagnosed with depression with those with other psychopathologies in addition to healthy controls. Third, the cross-sectional design limits causal interpretation. Lastly, former smoking status, current physical activity, and the evaluation of the menstrual phase could have provided a clearer perspective on AS.

This study is the first study investigating the relationship between insecure attachment and AS in adults. Since this is an exploratory study, the findings should be considered hypothesis generating. Our results demonstrated that neither active clinical depression alone nor childhood trauma nor insecure attachment are related to AS severity when we eliminate the clinical cardiovascular risk factors directly related to AS. In addition, we provided initial evidence regarding the positive relationship between insecure attachment and AS severity in healthy adults. Existing studies measured AS through different methods such as central AI [3], AI [14], ba-PWV [6,17], cf-PWV [16,18], AS index [15], and ankle-brachial index [19]. However, it is hard to gather these non-homogenous data; our results may support the data that psychological stressors and clinical depression may increase AS, not directly, but through clinical cardiovascular risk factors resulting from unhealthy behaviors [15,55].

5. Conclusion

This study offers new insights into the lack of association between psychological factors and AS severity in depressed individuals without clinically detectable core cardiovascular risk factors. Additionally, it provides initial evidence that insecure attachment patterns may be associated with AS severity in healthy individuals. These preliminary findings warrant further replication in larger and more representative samples. For future studies, it may be an important research topic to investigate whether insecure attachment patterns predict the increased AS severity independently of clinical depression and other psychological factors. Understanding the role of psychological factors in the development of AS may help us to design early intervention methods for modifiable risk factors of CVD and to prevent CVD-related morbidity and mortality.

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Authorship

All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

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Declaration of Competing Interest

No conflict of interest exists.

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