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Stress-coping skills and neuroticism in apical ballooning syndrome (Takotsubo/stress cardiomyopathy)

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ABSTRACT

Introduction: Apical ballooning syndrome (ABS) is typically associated with an antecedent stressful situation. Affected patients have been reported to have higher frequencies of premorbid affective disorders. We hypothesised that patients with ABS would have elevated levels of neuroticism (tendency to experience negative affect) and greater vulnerability to stress.

Methods: In this cross-sectional study, all active participants in the Mayo Clinic ABS prospective follow-up registry were invited to complete the third edition of the NEO Personality Inventory (NEO-PI-3). The NEO-PI-3 is the universally accepted measure of the 'Five-Factor Model' of personality. Inventory responses were scored using the NEO-PI-3 computer program and the data were compared with US normative sample used in standardisation of the inventory. Significance was set at 0.0014 to account for multiple comparisons.

Results: Of 106 registry participants approached, 53 completed the inventory. There was no difference in age, gender, time from ABS diagnosis, type of antecedent stressor (emotional, physical or none) or severity of initial illness between the responders and non-responders. Responders had mean Neuroticism T-scores of 48.0±10.6 (95% CI 45.1 to 50.9); p=0.18, when compared with the normal mean of 50. There was also no significant difference in the facet scale of Vulnerability: 46.9±8.4 (44.6 to 49.2), p=0.038, at α=0.0014.

Conclusions: Contrary to our hypothesis, patients with ABS do not manifest higher levels of neuroticism and do not have greater vulnerability to stress than the general population. These findings have implications for the clinicians' perception of, and approach to, patients with ABS.

KEY QUESTIONS

What is already known about this subject?

- Patients with apical ballooning syndrome (ABS) have been found to have a higher prevalence of affective disorders which are associated with high neuroticism (trait anxiety). This raises the question of whether a specific personality profile renders a subject prone to the development of ABS. A recent study suggests a high prevalence of 'type D' personality, which may be characterised by high neuroticism, but the 'type D' personality is not a universally accepted personality construct.

What does this study add?

- We found that patients with ABS do not demonstrate high levels of neuroticism, and thus do not seem to have a personality characterised by a predisposition to affective disorders. Additionally, there has been no study to date that has systematically assessed personality profiles of patients with ABS. This study addresses this gap in the literature.

How might this impact on clinical practice?

- The association of ABS with stressful situations, especially psychologically stressful situations, might tempt clinicians into assuming an underlying 'neurotic' personality and presume poor stress-coping skills. Our study refutes this, suggesting excessive stress exposure as the likely predominant causal variable. Attention should focus on evaluating and mitigating stressors in patients with a prior history of ABS. The demonstration that individuals developing ABS have, in general, a personality profile that lies within the limits of normal may promote accurate clinician perceptions and improve clinician–patient relationships.

INTRODUCTION

Apical ballooning syndrome (ABS), also known as Takotsubo or stress cardiomyopathy/syndrome, is a reversible cardiomyopathy typically characterised by transient systolic dysfunction of the mid and apical segments of the left ventricle.[1] The clinical presentation of ABS mimics an acute myocardial infarction, but obstructive coronary artery disease is typically absent. ABS is predominantly diagnosed in postmenopausal women and is preceded by an acute physical or emotional stress trigger in greater than two-thirds of patients.[2] Purported pathophysiological mechanisms underlying ABS

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include altered β adrenergic signalling in the presence of elevated catecholamine levels[3] and impaired vascular responses to stress.[4]

Aside from physiological factors, patients diagnosed with ABS may have a psychosocial predisposition to ABS. They are more likely to have a premorbid diagnosis of a chronic anxiety disorder compared with age-matched and gender-matched acute coronary syndrome and general population controls.[5–7] They are more likely to have a family history of anxiety or depression and more likely to report social stressors such as being divorced and isolated.[5] Intriguingly, patients with ABS appear to have a higher frequency of migraine and Raynaud's phenomenon.[8] ABS, migraine and Raynaud's share similarities with female predominance, precipitation by triggers, altered vascular reactivity and increased likelihood of affective disorders.[9] Of note, patients with migraine and Raynaud's who have no diagnosis of affective disorders, appear to have elevated levels of neuroticism, a normal personality trait defined as a propensity to experience negative affect that is expressed as nervousness and insecurity.[10 11] Elevated levels of neuroticism are found in patients with chest pain syndromes in the absence of coronary disease, and in those with increased cardiovascular mortality.[12] The association of neuroticism with migraine, Raynaud's and other cardiovascular diseases led us to postulate that ABS might be associated with elevated levels of neuroticism. Thus, our hypothesis was that patients with ABS would manifest a personality profile characterised by high neuroticism, compared with that of the general population. Our secondary hypothesis was that participants' vulnerability to stress would be significantly greater than in the general population.

PATIENTS AND METHODS

Participants

The Mayo Clinic Institutional Review Board approved the study protocol. Participants gave signed consent to participate in the study. This cross-sectional study utilised participants in the Mayo Clinic ABS Registry who are prospectively diagnosed with ABS at the time of presentation with their acute illness, and consent to participation in a registry. Enrolment in the registry requires that the Mayo Clinic diagnostic criteria for ABS are met, and includes the administration of a standardised questionnaire.[2] Annual follow-up is conducted with a completion of a health status questionnaire. Inclusion criteria for the current study were the following: adults (18 years or older), and who were able to read English at a sixth grade level (as the personality inventory is self-administered and written in English). Patients were excluded from the study if they had been withdrawn from the ABS registry, predominantly (seven of nine) due to dementia or brain injury.

Personality assessment

The third edition of the NEO Personality Inventory (NEO-PI-3) is the most rigorously validated and universally used inventory of normal personality.[13] It has become the standard inventory that measures the Five-Factor Model (FFM) and provides a systematic assessment of emotional, interpersonal, experiential, attitudinal and motivational styles. According to the FFM, the five major domains (also called factors) of personality are neuroticism, extraversion, openness, agreeableness and conscientiousness.[14] For clarity of presentation, when a personality *factor* is being discussed, that is, neuroticism, the word is not capitalised. However, when a domain (factor) or facet *scale* of the NEO-PI-3 is discussed, the *scale* title is capitalised, that is, Neuroticism, Vulnerability, etc. In addition, the NEO-PI-3 measures six underlying facets for each of the five domains. Taken together, the five domain scales and 30 facet scales of the NEO-PI-3 facilitate a comprehensive and detailed assessment of normal adult personality. The NEO-PI-3 is self-administered, requires a sixth grade reading level, uses a five-point Likert scale format, and has 240 personality and 3 validity items.

The focus of this study was on the neuroticism domain. This domain contrasts adjustment and emotional stability with maladjustment and identifies individuals who are prone to psychological distress and maladaptive-coping responses. The six facets of the Neuroticism scale are Anxiety (prone to worry, fearful, apprehensive), Angry hostility (tendency to experience anger and related states such as frustration and bitterness), Depression (prone to feelings of guilt, sadness, and loneliness), Self-consciousness (sensitive to ridicule, prone to feelings of inferiority), Impulsiveness (inability to control cravings and urges) and Vulnerability (difficulty coping with stress).

Feedback

The NEO-PI-3 was mailed to participants with a letter explaining the purpose of the study. In order to encourage participation, participants were offered the option of receiving the results of their testing in the form of the NEO-PDR Individual Planning Report (NEO-PDR; http://www4.parinc.com/WebUploads/samplerpts/NEO_PDR_Indiv_Rpt.pdf). The NEO-PDR consists of a 15-page report that substitutes potentially emotionally laden terms such as 'anxiety' and 'impulsivity' (contained in the standard NEO-PI-3 professional printout) with more neutral terms such as 'worry' and 'self-indulgence'. It provides an easily understood description of participants' distinctive personality characteristics, and how these characteristics can be an advantage in some circumstances and a disadvantage in others. Receipt of the NEO-PDR was the only incentive for participants' participation in the study.

Scoring

The inventory responses were entered into the scoring programme by a professional trained psychometrist who was unaware of the purpose of the study. Participants' scores were compared with a contemporary normative

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sample used in the standardisation of the NEO-PI-3 questionnaire. The test manual indicates the standardisation sample consists of 635 individuals, 279 men and 356 women age 21–91 years. These participants were in five age ranges: 21–25 (119), 26–30 (99), 31–40 (59), 41–50 (155), 51–60 (100) and 61+(103). They resided in 29 states, with 63% in Pennsylvania and were predominantly Caucasian (92.6%).[13] Separate gender norms are not reported, as aggregate personality differences between genders is minimal compared with that within genders.[15]

The normal mean T-score for each scale is 50; SD is 10. As per the NEO-PI-3 test manual, clinically significant T-scores are considered to be 5 points or more from the mean (≤45 or ≥55).[13] A patient with a neuroticism score of 55 or more is therefore considered to have high neuroticism.

Statistical methods

Responses and scores are summarised as mean±SD or frequency (%), as appropriate. Between-group comparisons were conducted using Student t test. A sensitivity analysis was completed to assess the potential impact of non-response bias. Clinical characteristics, including an index of severity of illness on presentation (Mayo Clinic risk score, see table 1 for scoring system),[16] are compared between participants who returned questionnaires (responders) and those who did not (non-responders) using Student t test for continuous variables and Pearson's χ^2 test for categorical variables. Where the domain and facet scores are compared between groups, a Bonferroni correction was applied to account for multiple comparisons (35 in total), thus giving a rejection region of p<0.05/35=0.0014.

Table 1 Characteristics of participants who returned questionnaires (responders) versus those who did not (non-responders)

Variable	Responders (n=53)	Non-responders (n=53)	p Value
Age	71.1±10.3	70.9±12.1	0.93
Male	2 (3.8%)	2 (3.8%)	1.0
Years since ABS presentation	4.9±2.7	5.0±2.6	0.94
Risk score >1*	26 (54.2%)	28 (52.8%)	0.89
Any stressor identified	31 (58.5%)	38 (71.0%)	0.15
Emotional stressor	15 (28.3%)	17 (32.1%)	0.67
ABS recurrence	3 (5.7%)	4 (7.6%)	0.70

Results presented as mean±SD or number (%).
*(Mayo Clinic) risk score: 1 point each for the following components: age >70 years; presence of physical stressor; ejection fraction <40% on first presentation. Scores of 1, 2 or 3 points are associated with a 28%, 58% or 85% risk of acute heart failure, respectively.[16]
ABS, apical ballooning syndrome.

RESULTS

The NEO-PI-3 was mailed to the 106 participants who met the inclusion criteria. Sixty-one inventories were returned, 53 completed, 1 started but incomplete and 7 declined consent. The remainder did not respond to participate in the study despite reminder letters.

Table 1 demonstrates the characteristics of the participants who completed the NEO-PI-3 compared with non-responders. Participants were primarily older women, evaluated on average 4.9 years after their ABS episode. There were no differences in age, gender, time since ABS occurrence, risk score, presence of an emotional stressor as a trigger (emotional triggering) or ABS recurrence between the groups.

Table 2 gives neuroticism domain and neuroticism facet scores for the 53 responders. ABS participants demonstrate no difference in neuroticism compared with the normal population: mean T-score 48.0±10.6 (95% CI 45.1 to 50.9), p=0.18, when compared with a population mean of 50. There was also no difference in the facet scales at the significance level of 0.0014.

Participants who demonstrated emotional triggering showed no difference on the Neuroticism factor when compared with those without emotional triggering (table 3). This was also true for participants who reported a physical stressor, compared with no physical stressor, or all stressors combined compared with no stressor. The three patients who had ABS recurrences had higher Neuroticism scores, 55.0±7.0 vs 47.6±10.7, in the group without recurrences, but this was not statistically significant (p=0.2).

The other 4 domain and 24 facet scales are contained in online supplementary table S1. While these scales were not the focus of our hypotheses and the current discussion, they are provided as an aid in further understanding the personality characteristics of our sample. ABS participants had similar scores to the normative sample on the domains of Openness, Conscientiousness

Table 2 Neuroticism domain and facet T-scores of the 53 participants compared with the normal population

Variable	T-scores	p Value
Neuroticism factor	48.0±10.6 (45.1 to 50.9)	0.18
Neuroticism facets		
Anxiety	49.6± 9.5 (47.0 to 52.3)	0.79
Angry hostility	45.7±10.9 (42.6 to 48.8)	0.0072
Depression	49.4±10.1 (46.6 to 52.2)	0.69
Self-consciousness	49.0±9.6 (46.4 to 51.7)	0.48
Impulsiveness	46.3±8.8 (43.9 to 48.7)	0.0034
Vulnerability	46.9±8.4 (44.6 to 49.2)	0.0094

T-scores are presented as mean±SD (95% CIs). The normal mean T-score for each scale is 50±10.

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Table 3 Neuroticism scores by stressor (N=53)

	Yes		No		
	n (%)	T-scores	n (%)	T-scores	p Value
Stressor reported	31 (58%)	46.3±10.5	22 (42%)	50.4±10.5	0.17
Emotional stressor	15 (28%)	44.4±10.6*	38 (72%)	49.4±10.4	0.13
Physical stressor	16 (30%)	48.1±10.5	37 (70%)	47.9±10.8	0.96

Scores reported as mean±SD; the normal mean T-score for each scale is 50±10.
*Clinically significant scores are ≤45 or ≥55.

and Extraversion, but had significantly higher scores on Agreeableness.

A sensitivity analysis was performed to determine the effect of non-responder bias on the mean Neuroticism score. A mean score of 62.0 among the 53 non-responders would be required to increase the mean score to 55 (a clinically significant Neuroticism score).

DISCUSSION

This study shows that patients with a history of ABS do not demonstrate higher levels of neuroticism compared with the normal population. Additionally, vulnerability to stress, as measured on the Vulnerability scale, is similar to the general population. None of the other Neuroticism facet scores were statistically different from the normative sample.

These findings are seemingly at odds with studies demonstrating that patients with ABS have higher rates of diagnoses of anxiety and depression,[5 6] as both of these diagnoses are correlated with elevated levels of neuroticism. A key feature of most reports of ABS is the clear association of a stressor with the onset of symptoms,[2] but studies reporting high levels of affective disorders also report higher levels of ongoing life stressors in patients with ABS.[5] Cumulative stress exposure across the lifespan is associated with an increased risk for depression, and though this effect is potentiated by high neuroticism, this does not require its presence to increase depression risk.[17] In the context of the present study, a potential common feature between chronic affective disorders and ABS could be ongoing exposure to excessive levels of stress, rather than a maladaptive response to stress. Patients with ABS have also been shown to have impaired vascular responses to mental stress.[4] Our findings might suggest that an individual's physiological response to stress, rather than their perception of the stress, may the substrate for ABS.

Our findings contrast with those obtained by Compare *et al*.[18] This group evaluated participants with ABS secondary to emotional triggering and found a higher proportion of type D personality, 3 months after the acute presentation, compared with those without emotional triggering. Type D (distressed) personality is characterised by high negative affectivity (NA, tendency to experience negative emotions) and high social inhibition (SI, tendency to inhibit the expression of emotions/behaviours in social interactions to avoid disapproval).[19] The NA and SI constructs in the type D model would appear to be reflected by the Neuroticism factor and the Self-consciousness facet scales on the NEO-PI-3. There have been multiple criticisms of the validity of the type D construct, especially in the dichotomisation of its two variables.[20 21] Additionally, type D personality is assessed by the Type D scale-14, which was validated against the NEO-Five-Factor Inventory (FFI). The NEO-FFI measures only the five major domains of the FFM,[19] and as the abbreviated version of the full NEO-PI-3, has reduced fidelity. Abbreviated scales provide only approximate assessments of complex personality constructs.

Another study by Del Pace *et al*[22] evaluated the presence of high-anxiety trait, defined as a score ≥40 on the Spielberger Trait Anxiety Inventory (STAI) scale, in patients with ABS compared with age, gender and patients with hypertension-matched ST elevation myocardial infarction (STEMI). They found that high-anxiety trait was common in patients with ABS (60%), but no different than patients with STEMI (52%).

It is important to recognise the difference between anxiety as a 'trait' versus an anxiety 'state'. In the field of personality assessment, traits are conceptualised as stable personality dispositions that are relatively invariant across situations, and that have a significant biological substrate. Conversely, *states* are transient emotional reactions that are highly sensitive to the situational context.[23] Del Pace studied patients during the index hospitalisation, and in the Compare study, evaluation was done at 3 months following ABS. In both of these cases, the findings may have been reflective of ongoing life stressors that were associated with the index event (a 'state') rather than an intrinsic personality trait. Indeed, Compare *et al*[24] subsequently reported persistence of negative psychological impact of the episode of ABS up to 1 year. Therefore, a strength of the current study is that participants were assessed on average, 5 years after the episode of ABS.

Stress-coping skills

The findings of our study with respect to the second hypothesis regarding vulnerability to stress in patients with ABS are in accord with recent literature. Kastaun *et al*[25] compared women with ABS to patients with age-matched non-STEMI and heart-healthy female controls

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18.4±8.5 months following the index event. They found no significant difference among the groups in the Freiburger Personality Inventory-revised (FPI-R), the Symptom Checklist revised (SCL-90-R) and the Trier Inventory for the Assessment of Chronic Stress. A further report by the same group on the same participants assessed the personality trait 'locus of control'. Internal versus external locus of control influences how patients cope with stress.[26] There were no differences between patients with ABS and controls. Another series of studies from a single group evaluating stress-coping strategies using the Stressverarbeitungsbogen-120 (SVF-120)[27 28] reported more unfavourable stress management strategies in patients with ABS compared with normal controls,[27] but no difference when compared with patients with acute coronary syndrome.[28] Given these conflicting findings, the authors were doubtful that routine assessment of stress-coping strategies in patients with ABS would be of significant benefit, a conclusion which is strengthened by our study findings.

Female gender and physicians' perceptions

We have outlined the route to the development of our hypothesis of high neuroticism. However, with the female predominance of this condition (96% in our series), one must acknowledge the possibility of subconscious bias which has been ubiquitous in the medical literature. Women have been perceived to be more emotionally labile than men and are thought to more likely to somaticise emotional upsets as physical problems.[29] Indeed, these perceptions may be responsible for significant delay in diagnosis and appropriate management in women in cardiovascular disease studies.[30] Physicians have also been shown to judge women's problems as being more likely to be influenced by emotional factors, than men's,[29] a perception which is particularly relevant to the diagnosis of ABS.

Limitations

There are some limitations to our study. The decision by a participant to enrol in a research study is determined to some extent by their personality. For instance, our participants scored significantly higher than the norm (>55) on the scale of Agreeableness. One might postulate a propensity for participants with high neuroticism to avoid enrolment for a variety of reasons including worry about the safety of their data. However, the range of Neuroticism scores in this study was 27–73, showing that even participants with very high Neuroticism scores were included. We calculated that the mean score that the non-responders would have to have would be 62.0 in order to shift the mean Neuroticism score into the high range, which is exceedingly unlikely. Our participants were from a predominantly white (98%), American, Midwest population. This percentage is greater than the 92% Caucasian in the NEO-PI-3 normative sample. Hence, the results may be less generalisable to a population of a different racial or cultural background or nationality. The adult NEO-PI-3 norms consist of a combined gender sample, with 16% of this adult sample being greater than 61 years. Using a comparison sample of similarly aged women may yield additional insights about unique personality characteristics in this group compared with the general adult population the NEO-PI-3 norms are designed to reflect. However, it is worth noting that in longitudinal studies, personality is a relatively stable characteristic beyond the age of 30 years.[31] The size of the study is also a limitation; however, our sample was larger than many similar studies. Although a clinical comparison group, such as myocardial infarction controls, was not available, we were able to compare our cohort with a large sample size of a 'normal' population.

CONCLUSION

Patients with ABS do not manifest higher levels of neuroticism and do not manifest poor stress-coping skills compared with the general population. This finding should be borne in mind in the approach to the long-term management of the patient with ABS. Given the relationship of ABS with acute stressors, clinicians might be tempted to focus on easily implemented interventions such as pharmacotherapy or psychotherapy. This study suggests that in the absence of psychiatric disorders or an acute anxiety state, an individualised approach to psychosocial intervention that addresses acute and potentially chronic stressors may be more appropriate to prevent recurrence.

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