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# Cortisol awakening response is elevated in acute coronary syndrome patients with type-D personality

Daisy L. Whitehead, Linda Perkins-Porras, Philip C. Strike, Kesson Magid, Andrew Steptoe*

*Department of Epidemiology and Public Health, Psychobiology Group, University College London, London, United Kingdom*

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**Abstract**

**Objective:** Type-D or "distressed" personality and depression following admission for acute coronary syndrome (ACS) have been associated with poor clinical outcome. The biological pathways underpinning this relationship may include disruption of the hypothalamic–pituitary–adrenocortical (HPA) axis. We therefore assessed cortisol output in patients who had recently suffered from ACS. **Method:** Salivary cortisol was assessed eight times over a 24-h period in 72 patients within 5 days of admission for ACS. Depressive symptoms were measured with the Beck Depression Inventory (BDI), and type-D personality was measured with the Type-D Scale-16. Particular attention was given to cortisol awakening response (CAR), which was measured as the difference in cortisol between waking and peak responses 15–30 min later. **Results:** Cortisol showed a typical diurnal pattern, with low levels in the evening, high levels early in the day, and CAR averaging 7.58±10.0 nmol/l. Cortisol was not related to the severity of ACS or underlying coronary artery disease or to BDI scores. The CAR was positively associated with type-D personality independently of age, gender, and body mass ($P$=.007). Linear regression showed that type-D personality accounted for 7.9% of the variance in CAR after age, sex, body mass, BDI, cortisol level on waking, and fatigue had been taken into account ($P$=.008). **Conclusions:** Type-D personality may be associated with disruption of HPA axis function in survivors of acute cardiac events and may contribute to heightened inflammatory responses influencing future cardiac morbidity.


*Keywords:* Type-D personality; Depression; Fatigue; Cortisol; Acute coronary syndrome; Coronary heart disease

## Introduction

Negative affective states are robust predictors of susceptibility to and morbidity from coronary heart disease (CHD), even after controlling for traditional risk factors [1,2]. Type-D personality and depression both predict poor prognosis in individuals following acute coronary syndrome (ACS). The pathways underpinning these relationships are not yet fully understood. This article investigated the relationship between psychological status and hypothalamic–pituitary–adrenocortical (HPA) axis function by assessing salivary cortisol repeatedly through the evening, early morning, and the remainder of the day in patients hospitalized with ACS.

Depressive symptoms and clinical depression in the days following the occurrence of ACS have been associated with increased mortality, revascularization, and impaired quality of life in a number of studies, independently of clinical risk factors [3–5]. Type-D personality [6] is a relatively recent psychological construct focusing on traits of negative affectivity and lack of emotional expression in social situations. It differs from acute symptoms of affective distress in being regarded as relatively stable over time and has been shown to predict adverse clinical outcomes in patients following ACS, individuals who have undergone revascularization, and patients with heart failure [6–9]. Both the negative affectivity and social inhibition components of type-D appear to be important, acting synergistically to predict morbidity.

* Corresponding author. Department of Epidemiology and Public Health, Psychobiology Group, University College London, London WC1E 6BT, United Kingdom.

*E-mail address:* a.steptoe@ucl.ac.uk (A. Steptoe).

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Several pathways that potentially relate negative affective states with CHD are being evaluated, including disturbances in inflammatory responses, autonomic imbalance, and behavioral responses such as poor adherence [10–12]. Dysregulation of neuroendocrine function is another plausible pathway through which depressive symptoms and type-D personality might influence cardiovascular health [13,14]. HPA axis dysregulation, resulting in elevated cortisol levels and loss of normal homeostatic negative feedback mechanisms, has been associated with hypertension, changes in body composition, hyperlipidemia, insulin resistance, impaired endothelial dysfunction, changes in hemostatic factors, and, if sustained over a long period, increase in the activity of proinflammatory cytokines [15]. One recent clinical study found that morning cortisol levels were positively associated with degree of stenosis on angiogram in women 3–6 months following ACS [16], and a prospective association between cortisol/testosterone ratio in men and the development of fatal and nonfatal CHD has been described [17].

Cortisol shows a robust diurnal pattern in healthy adults (peaking at 20–45 min after waking) and then steadily decreases through the day, with the lowest levels during the night and in the early morning. The increase in cortisol following waking is known as cortisol awakening response (CAR) and is largely independent of the underlying diurnal signal [18]. Elevated morning cortisol is a risk factor for clinical depression [19,20], and a larger CAR is associated with depressive symptoms [21], low positive affect [22], high levels of perceived stress [23], and chronic job stress [24]. Smaller CARs have been observed in patients suffering from chronic fatigue [25] and in volunteers with self-reported health problems and chronic diseases [26].

Only one study to date has investigated the association of cortisol with depressive symptoms in a CHD population. Otte et al. [27] found a greater 24-h cortisol output in depressed outpatients with CHD than in nondepressed patients, independently of cardiac disease severity. However, the protocol used for cortisol sampling did not allow the subtleties of daily cortisol profile to be analyzed, and participants were all outpatients. No study has investigated cortisol and type-D personality in a CHD population, although one study found an association of greater cortisol reactivity with laboratory stressors in healthy volunteers [28]. Nor have the cortisol profiles of patients in the immediate aftermath of ACS been assessed.

The current study investigated salivary cortisol sampled several times over a 24-h period in patients hospitalized for ACS. We specifically focused on CAR as a dynamic measure that has been shown to be sensitive to psychosocial factors. Based on the previous literature, we hypothesized that the magnitude of CAR would be positively associated with levels of depression and type-D personality in patients following ACS, independently of other predictors of cortisol function such as age, sex, body mass index (BMI), and clinical factors.

## Methods

### *Participants*

Participants were recruited from four London hospitals within 5 days of admission as part of a larger study described elsewhere [29]. All patients were aged between 20 and 80 years old, with a diagnosis of ACS confirmed by electrocardiogram (ECG) changes (namely, new ST elevation of >0.2 mV in two contiguous leads in leads $V_1$, $V_2$, or $V_3$, and new ST elevation of >0.1 mV in two other contiguous leads; ST depression of >0.1 mV in two contiguous leads in the absence of any QRS confounders, new left branch block, or dynamic T-wave inversion in more than one lead) or cardiac enzymes (troponin T measurement of >0.1 μg/l and/or a creatine kinase measurement more than twice the upper normal range for the measuring laboratory) [30]. Exclusion criteria were renal impairment, neurological or severe psychiatric illness, and inability to complete either interview or questionnaire measures of psychological status. For cortisol sampling, we excluded patients with ongoing infection or inflammatory illness and those taking corticosteroid medications. The sample consisted of 76 patients who agreed to provide eight saliva samples for cortisol analyses. Seventy-four individuals provided the full eight samples, of whom two were excluded as their waking cortisol samples were taken very early in the morning before natural waking, leaving a final sample size of 72.

### *Clinical data*

The following clinical data were collected: age, BMI, type of ACS [ST elevation myocardial infarction (MI) vs. non-ST elevation MI or unstable angina], type and location of ECG changes, peak levels of cardiac enzymes troponin T and/or creatine kinase, number of diseased vessels on angiogram, history of diabetes mellitus, hypertension, and smoking. A composite index of cardiac risk over 6 months was also computed using the algorithm developed in the Global Registry of Acute Coronary Events (GRACE) study, an international investigation of 17,142 admissions for ACS in 14 countries [31]. The algorithm includes nine variables (older age, history of MI, history of heart failure, increased pulse rate at presentation, lower systolic blood pressure at presentation, elevated initial serum creatinine level, elevated initial serum cardiac biomarker levels, ST segment depression on presenting ECG, and nonperformance of percutaneous coronary intervention in hospital), which are weighted to generate the risk score.

### *Psychological data*

Measures of depression and type-D personality in the days following admission were obtained using self-report questionnaires. Depression was measured using the Beck Depression Inventory (BDI) [32], a 21-item questionnaire