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The associations between diurnal cortisol patterns, self-perceived social support, and sleep behavior in Chinese breast cancer patients

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Summary

Objective: This study examined the relationships between diurnal cortisol patterns and sleep behavior, social support, psychological factors, and perceived health status in breast cancer patients.

Methods: One hundred and eighty-one breast cancer patients completed a self-report questionnaire that combined the Hospital Anxiety and Depression Scale, the Yale Social Support Scale, and self-perceived measures of physical health, stress, sleep quality, total sleep hours, and time of awakening. Salivary cortisol was collected upon waking, at 1200 h, 1700 h, and 2100 h on two consecutive days. Multiple regression analysis was performed on the diurnal cortisol slope that was derived from slope analysis of the log-transformed cortisol data.

Results: Controlling for the initial cortisol level, a flatter diurnal cortisol slope was significantly associated with a later time of awakening, higher negative social support, poorer perceived health, poorer sleep quality, and shorter total sleep hours. Anxiety and depression were not significantly correlated with the slope.

Conclusions: The results indicate a subtle dysregulation in hypothalamic-pituitary-adrenal axis functioning in patients with highly negative social support, poor perceived health, poor sleep quality, a later time of awakening, and insufficient sleep hours.

1. Introduction

The hypothalamic-pituitary-adrenal (HPA) axis plays an important role in stress regulation; cortisol is its hormonal end product (Gunnar and Quevedo, 2007). Cortisol secretion

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typically exhibits a circadian rhythm with a early-morning peak followed by a gradual decline and a late-evening trough (Stone et al., 2001). In patients with breast cancer, aberrant diurnal cortisol patterns have been found in the form of a lower early-morning peak and a slower decline (Touitou et al., 1996). The altered rhythm, as a manifestation of anomalous activity of the HPA axis, is linked to outcomes such as fatigue, depression and early mortality (Sephton et al., 2000; Bower et al., 2005; McGregor & Antoni, 2009). As Abercrombie et al. (2004) noted, the prognostic value of the diurnal rhythm suggests that investigation into the associated physiological and psychological factors is warranted.

Disturbances in sleep behavior such as poor sleep quality, insomnia, and early awakening are important concerns among breast cancer patients (Davidson et al., 2002; Lee et al., 2004). Whereas one previous study of breast cancer patients (Sephton et al., 2000) showed more frequent nocturnal awakenings to be linked to higher nocturnal cortisol levels, another study (Carlson et al., 2007) found no association between sleep quality or sleep duration and the diurnal cortisol slope. For psychological factors, social support has been shown to be a protective factor against mortality risks in breast cancer patients (Trunzo & Pinto, 2003; Friedman et al., 2006; Kroenke et al., 2006). Despite the demonstrated reciprocal relationship between psychological and physiological functioning in general (Bauer, 1994), two previous studies of metastatic breast cancer patients (Turner-Cobb et al., 2000; Abercrombie et al., 2004) found no significant associations between social support and HPA axis functioning.

In general, the small sample sizes in previous studies of the relationships between diurnal cortisol patterns and sleep behavior or social support have led to a lack of statistical power, thus rendering the results inconclusive. To address this issue, we conducted a cross-sectional study with a sample of 181 breast cancer patients to explore the relationships between diurnal cortisol patterns, social support, and sleep behavior. Specifically, we hypothesized that (1) breast cancer patients with a higher level of negative social support or a lower level of positive social support would show a flattened diurnal cortisol slope and (2) patients who reported better sleep behavior, in terms of better sleep quality, earlier time of awakening, and longer total sleep hours would show a steeper diurnal cortisol slope.

2. Methods

2.1. Subjects and procedures

This study recruited 181 breast cancer patients from four cancer resource centers in Hong Kong using letters and phone calls. During the screening interview, the study's purposes, risks, and benefits were explained to the participants, who then provided written informed consents. They were instructed to complete the self-report questionnaire and to collect salivary cortisol measurements at home. Ethical approval was obtained from a local institutional review board. The exclusion criteria were metastases and recurrence of breast cancer, a history of major psychiatric illness, pregnancy, and inability to read Chinese.

2.2. Measures

2.2.1. Anxiety and depression

The Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983; Leung et al., 1999) is a 14-item 4-point Likert scale that assesses anxiety (7 items) and depression (7 items). The subscale score is classified into four categories: normal = 0–7, mild = 8–10, moderate = 11–14, and severe = 15–21. In this study, the scale had good Cronbach's alpha scores of 0.86 and 0.75 for the anxiety and depression subscales, respectively.

2.2.2. Social support

The Yale Social Support Index (Seeman and Berkman, 1988) assesses the perceived quantity and quality of positive social support (3 items) and negative social support (3 items) for cancer patients, with higher scores indicating greater degrees of both. In this study, the scale had Cronbach's alpha scores of 0.58 and 0.62 for positive and negative social support, respectively.

2.2.3. Salivary cortisol

Participants used Salivette tubes to collect saliva samples at four time-points on two consecutive days: wake-up, 1200 h, 1700 h, and 2100 h. The mean (SD) collection time was 0719 h (70 min), 1225 h (42 min), 1729 h (39 min), and 2136 h (40 min). Four data points were excluded upon screening for outliers in collection times (>4 SD deviation from mean). The participants were reminded not to brush their teeth or eat prior to sample collection to avoid contamination and were advised to follow their normal daily routines otherwise. Collected tubes were kept frozen until they underwent laboratory analysis of the salivary cortisol using an enzyme-linked immunoassay kit (Salimetrics, PA, USA). The intra-assay and inter-assay coefficients of variation were 3% and 10%.

2.2.4. Sleep behavior and other measures

The participants also used a 10-point scale (a score of five indicating level or condition same as usual, with a score above five indicating higher than usual) to evaluate self-perceived levels of health, stress, and sleep quality. Information on time of awakening and total sleep hours was also reported.

2.3. Statistical analysis

The slope analysis was carried out on the four cortisol measurements (Abercrombie et al., 2004; Vedhara et al., 2006). The raw cortisol data displayed considerable skewness (0.76–2.00) and kurtosis (0.28–6.16). Preliminary analyses showed no significant differences in the cortisol measurements across days ($t = 0.11$–1.67, $p > 0.05$). Thus, the data were log-transformed and aggregated across days in the slope analysis, which regressed the log-transformed data on the four measurement occasions to produce the diurnal cortisol slope. A steeper (more negative) diurnal slope indicated a faster decline in cortisol, whereas a flatter (more positive) slope indicated a slower decline. Correlational and regression analyses were carried out between the diurnal cortisol slope and the study variables, namely, perceived health,