An investigation into medical and cancer-related factors that predict cortisol patterns among breast cancer survivors

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Background

- Breast cancer survivors (BCS) can exhibit hypothalamic-pituitary-adrenal (HPA) axis dysregulation, as indexed by abnormalities in cortisol concentration patterns.[1,2]
- HPA axis dysregulation is linked to negative health outcomes such as obesity, depression, pain, fatigue, and diabetes.[3,4]
- Medical and cancer-related variables such as menopausal status, body mass index (BMI), cancer stage, and the completion of chemotherapy have been linked to cortisol levels in different clinical populations including BCS.[5,6] However, associations have seldom been examined over time.
- Identifying these associations represent a step forward towards the identification of BCS at greater risks of physiological dysregulation after BC thereby informing intervention strategies for optimal post-treatment care.

Objectives

1. **Examine the diurnal cortisol patterns of BCS during the first year post-treatment.**
2. **Assess medical and cancer-related variables as predictors of the diurnal cortisol patterns of BCS.**

Methods

- **Participants**
  - 201 BCS;
  - M=10.6±3.4 months post-diagnosis at study inception; M_{age}=57.9 ± 10.7 years; 92% White; 56% married; 64% post-menopausal; M_{BMI}=26.31 kg/m^2.
- **Procedures & Measures**
  - **Diurnal cortisol***: Participants provided 5 saliva samples on 2 non-consecutive days at approximately 3.5 months post-treatment (T1) and again every 3 months thereafter (T2-T5).
    - Cortisol was assessed using commercially available highly-sensitive enzyme-linked immunosorbent assay (ELISA).[7]
    - The area under the curve (AUC) of diurnal cortisol secretion pattern was calculated for each day and the mean AUC for both days at each timepoint was used as main outcome.

      *Lower AUCs indicate less exposure to cortisol.
  - **Menopausal status, cancer stage, & treatment type**: Data on participants' medical and cancer-related characteristics were collected via self-report questionnaire completed at T1.
  - **BMI**: Height and weight were measured by a trained technician at T1, and used to compute BMI and categorize participants based on Health Canada BMI Chart.[8]
- **Data Analysis**
  - A 4-way RM-ANOVA was performed to examine between-group differences in cortisol AUCs based on menopausal status (pre- or post-menopausal), BMI category (underweight and normal or overweight and obese), cancer stage at diagnosis (I, II, or III) , and chemotherapy exposure (yes or no).

*References available upon request

Results

- ***Main effect of Time***: Mean diurnal cortisol AUCs of BCS differ significantly across time points [F(4,320)=6.13, p<.01, η_p^2=.07], whereby AUCs at T4 (M=9.82±0.33) were significantly lower than at T2 (M=11.46±0.35), T3 (M=10.95±0.29), and T5 (M=11.25±0.35), and AUCs at T1 (M=10.50±0.24) were significantly lower than T2 (M=11.46±0.35).
- ***Main effect of stage at diagnosis***: Mean diurnal cortisol AUCs significantly differ by stage [F(2,80)=4.19, p=.02, η_p^2=.10], wherein BCS diagnosed with stage III breast cancer (M=10.00±0.45) had significantly lower cortisol AUCs than BCS diagnosed with stage I breast cancer (M=11.60±0.35).
- ***Time and BMI interaction effect***: Changes in the diurnal cortisol AUCs of BCS over time were dependent on BMI [F(4,320)=4.10, p<.01, η_p^2=.05], wherein BCS with an underweight-to-normal BMI (M=10.56±0.29) had a significantly lower mean diurnal cortisol AUCs at T2 and at T5 than BCS with a overweight-to-obese BMI (M=11.06±0.34).
- ***Time and chemotherapy interaction effect***: Changes in the diurnal cortisol AUCs of BCS over time were dependent on chemotherapy exposure, [F(4,320)=4.76, p<.01, η_p^2=.06], wherein BCS who received chemotherapy (M=10.98±0.25) had a significantly higher mean diurnal cortisol AUCs at T3 and at T4 than BCS who did not received chemotherapy (M=10.55±0.40).

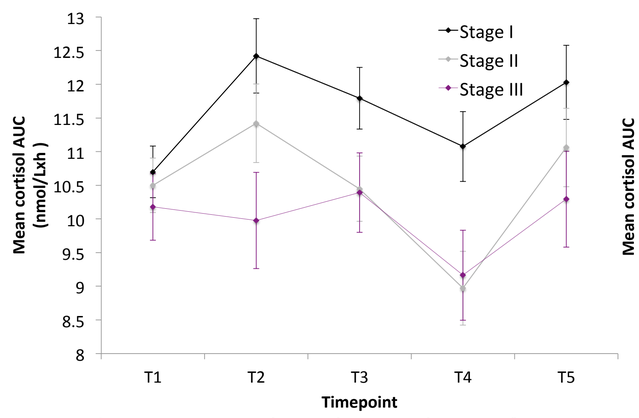

Figure 1. Mean diurnal cortisol AUC of participants over time by cancer stage.

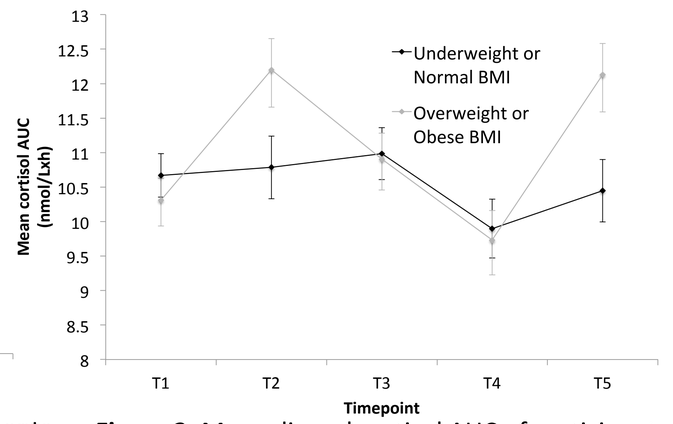

Figure 2. Mean diurnal cortisol AUC of participants over time by BMI classification.

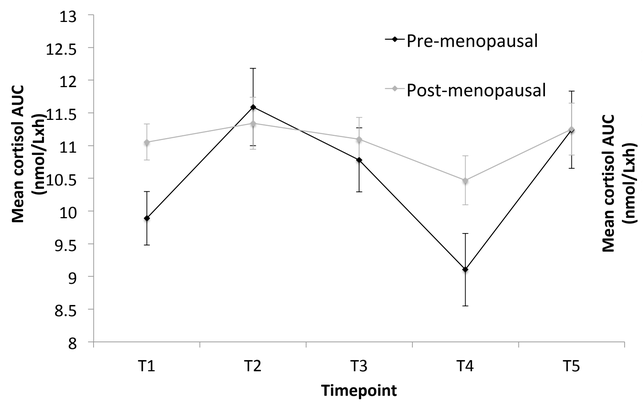

Figure 3. Mean diurnal cortisol AUC of participants over time by menopausal status.

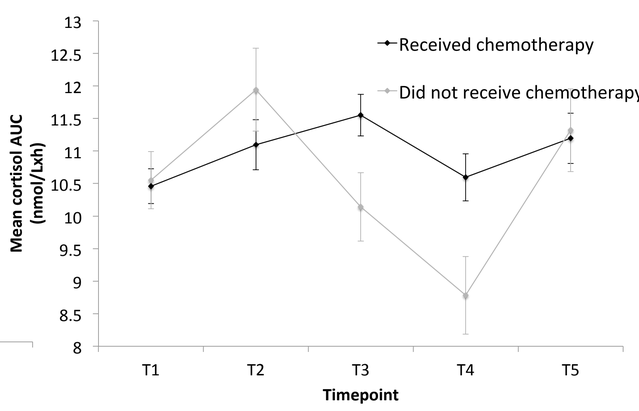

Figure 4. Mean diurnal cortisol AUC of participants over time by chemotherapy exposure.

Discussion & Conclusion

- Results suggest **stage of diagnosis**, **BMI**, and **chemotherapy exposure** are associated with cortisol concentration patterns among-BCS shortly after treatment completion.
- The association between higher initial stage of diagnosis and lower cortisol levels may reflect the impact of more intensive treatment procedures or perhaps suggest that tumor has a direct impact on the HPA axis.[9-11]
- The implications of the associations of BMI and chemotherapy with changes in the cortisol levels of BCS over time remain unclear. Future studies should investigate additional factors that may play a role in these associations such as physical activity, age, and time since diagnosis and examine these patterns of changes over longer periods of time.

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