Diurnal Variations of Pro-Tumorigenic Salivary Cytokines and Effects of Psycho-Physiological Stress in Gynecologic Cancer Patients and Controls

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INTRODUCTION

- Gynecologic (GYN) cancers account for over 116,000 new cancer diagnoses and 34,000 cancer-related deaths among American women annually.
- Research supports multi-directional associations among neuro-endocrine immunologic processes, circadian rhythms, psychological factors, and cancer outcomes.
- These associations are impactful for individuals with cancer given heightened susceptibility to stress-mediated cancer-related mortality.
- Via salivary biomarkers, these associations can be assessed using non-invasive methods that are cost-effective and ecologically sound.

STUDY PURPOSE

To examine diurnal circadian patterns of salivary pro-inflammatory beta (IL-6) and IL-1b and their relationships to psycho-physiological stress within individuals with GYN cancers and controls.

PARTICIPANTS

- CASES: Women with confirmed GYN malignancies scheduled to undergo surgical treatment who endorse sleep dysregulation.
- CONTROLS: Women with confirmed benign GYN disease scheduled to undergo surgical treatment who endorse sleep dysregulation.
- Cases and controls were matched on self-disclosed race and ethnicity.

METHODOLOGY

- **Study Design:** Longitudinal, non-experimental
- **Psychological stress:** was operationalized as participant-reported state and trait anxiety. Measured by the State and Trait Anxiety Index (STAI); greater STAI scores were consistent with greater state and trait anxiety
- **Physiological stress:** was operationalized as salivary cortisol slope, with flatter diurnal slopes consistent with greater chronic physiological stress.
- **Salivary collections:** were completed at home by participants on the three days leading up to their surgery via Salivettes®
- **Psychological stress:** was operationalized as participant-reported state and trait anxiety. Measured by the State and Trait Anxiety Inventory (STAI).
- **Salivary cytokines:** were quantified using Enzyme-Linked Immunosorbent Assay (ELISA) kits.

RESULTS

- **Surgical Methods**: Mixed linear models were performed to identify and compare IL-6 and IL-1b diurnal rhythms across cases and controls; robust regression analyses were performed to examine relations between psychophysiological stress and cytokine slopes.
- **Cytokine analyses**: demonstrated IL-6 decreased across the day in cases (negative slope) and controls (positive slope), while IL-1b increased throughout the day in both groups (positive slope).
- **Psychological stress**: reported state and trait anxiety. Measured by the State and Trait Anxiety Inventory (STAI).
- **Sample sizes**: and inclusion of a control group without overt cancer.
- **Future research**: is needed to elucidate current findings utilizing larger sample sizes and inclusion of a control group with non-Cancer disease.

CONCLUSION

- Overall findings are consistent with the belief that chronic stress adversely affects neuro-endocrine immunologic processes.
- This study is the first to demonstrate an association between higher trait anxiety and greater diurnal salivary IL-6 slope blunting within GYN populations, highlighting the utility of trait anxiety as a potential clinical screening indicator for identifying GYN patients at risk for negative outcomes.
- Evidence-based behavioral interventions for clinically significant anxiety may be improve health outcomes in this population.
- Future research is needed to elucidate current findings utilizing large sample sizes and inclusion of a control group without GYN disease.

REFERENCES