Assessing Cortisol Awakening Response in Women with Breast Cancer

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INTRODUCTION

- Fatigue, as measured by changes in cortisol levels, is one of the most common yet disregarded side effects of cancer and its treatment and may even affect the trajectory of treatment before the onset of treatment.[1]
- It has been found that cortisol awakening response (CAR) is a prospective risk factor of depressive symptoms in women after breast cancer treatment[2] so we aim to investigate its relationship with other biobehavioral variables before beginning treatment.
- CAR may be related to other demographic and biobehavioral factors which can help identify patients who may be in need of targeted intervention before beginning adjuvant treatment.

OBJECTIVES

- Assess the relationship between CAR and biobehavioral risk variables after controlling for demographics among women diagnosed with breast cancer before beginning adjuvant treatment.
- Identify which variables explain changes in CAR in this population and which are interesting for further study and targeted intervention.

METHODS

- We analyzed data from the RISE study on cancer-related fatigue. The original dataset was collected through a combination of interviews, blood collection, and chart review. The study sample consisted of 131 women who were diagnosed with breast cancer and had not started adjuvant therapy.
- We used bivariate and multivariate linear regressions to assess the relationship between cancer treatment type, biobehavioral risk variables, demographics, and CAR levels.
- Potential outliers were assessed using Cook's Distance, leverage, and studentized residuals. Sensitivity analysis was conducted to assess the effect of the potential outliers on the regression coefficients, but we did not remove any observations from our sample.
- Model selection was conducted by using Mallows Cp, AIC, and BIC to assess and rank our pool of candidate models.
- A quadratic specification for age was added to the final model based on component-plus-residual diagnostic plots (See Figure 2).

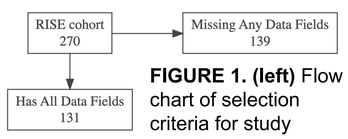

FIGURE 1. (left) Flow chart of selection criteria for study cohort not containing any missing data.

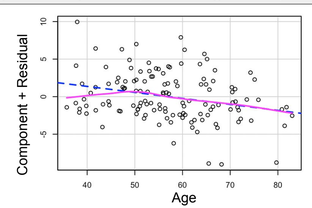

FIGURE 2. Component plus residual plot for 'AGE' showing a possible non-linear relationship.

RESULTS

1. Sample Baseline Characteristics

Variable	N	Mean	SD
CORTISOL.CAR.KRK	131	8.142	3.456
RACE2.STR	131		
... Non-White	31	23.7%	
... White	100	76.3%	
AGE.BL	131	57.067	10.897
EDUC3.STR	131		
... At most a high school degree	43	32.8%	
... College graduate	47	35.9%	
... Post-graduate degree	41	31.3%	
EMPLOY3.STR	131		
... Employed full-time	56	42.7%	
... Employed part-time	14	10.7%	
... Not employed	61	46.6%	
SMOKER	131		
... Current	2	1.5%	
... Former	39	29.8%	
... Never	90	68.7%	

Variable	N	Mean	SD
INCOME3.STR	131		
... 100,000 or more	78	59.5%	
... 60,000-$100,000	22	16.8%	
... Under $60,000	31	23.7%	
BMI.BL	131	25.398	5.783
MARRIED2	131	0.664	0.474
MENOSTATFINAL.BL.STR	131		
... Hysterectomy	8	6.1%	
... Peri-menopausal	8	6.1%	
... Post-menopausal	81	61.8%	
... Pre-menopausal	34	26%	
SPS_ATTACH_BL	131	15.053	1.711
FSI_AVG_BL	131	3.511	2.132
CTQ_WALKER_BIN_BL	131	0.412	0.494
PSMS_BL	131	22.099	4.513

Variable	N	Mean	SD
CHARLSON	131	0.313	0.596
GODIN_BL	131	27.431	21.567
RSES_BL	131	34.382	4.735
SCID_CURRMDD_BL	131	0.076	0.267
ALC_BIN	131		
... High drinking	43	32.8%	
... Moderate drinking	43	32.8%	
... No alcohol	45	34.4%	
KIDS_BIN	131		
... Kids	97	74%	
... No kids	34	26%	
SURGTYPE_ENROLLMENT_BIN	131		
... Lumpectomy	90	68.7%	
... Mastectomy	41	31.3%	

TABLE 1. The analysis cohort is mostly white (76.3%), never-smoking (68.7%), married (66.4%), with kids (74%), high-income (59.5% having income $100k or more), and postmenopausal (61.8%).The average baseline age is 57 years with average BMI of 25.4. Most of the cohort's surgery type is lumpectomy at 68.7%, with 31.3% having a mastectomy.

2. Model Selection

	Selection Criteria			Candidate Variables																								
	CP	AIC	BIC	RACE	EDU	INC	PSM	CHA	SCI	KID	AGE	AGE_sq	EMP	MAR	GOD	SMK	BMI	MENO	SPS	FSI	CTQ	RSE	ALC	SRG
	-0.01	707.35	761.98	x	x	x	x	x	x	x	x	x	x					x				x		
	0.11	709.51	767.01	x	x	x	x	x	x		x		x			x		x				x		
	0.17	706.05	754.92	x	x	x	x	x	x	x	x							x				x		
	0.24	709.15	769.53	x	x	x	x	x	x	x	x		x			x		x				x		
	0.44	708.37	760.13	x	x	x	x	x	x		x		x					x				x		
Full Model	13.84	724.07	810.33	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x

TABLE 2. Above are the top five models ordered by CP value. The model with the lowest CP value keeps the variables of race, education, income, Perlin-Schooler Mastery Scale, Charlson Comorbidity Index, current diagnosis of Major Depressive Disorder, kids, age, age squared, employment, menopausal status at baseline, and Rosenberg Self-Esteem scale at baseline.

3. Regression Output

	Bivariate			Multivariate		
	Beta	SE	P.Value	Beta	SE	P.Value
(Intercept)	NA	NA	NA	-6.425	10.742	0.551
RACE2: White	-0.291	0.713	0.684	0.188	0.768	0.807
EDUC3: College graduate	1.142	0.722	0.116	1.633	0.801	0.044
EDUC3: Post-graduate degree	1.558	0.747	0.039	1.949	0.843	0.022
INCOME3: 60,000-$100,000	-0.461	0.840	0.584	-0.194	0.861	0.822
INCOME3: Under $60,000	-0.362	0.738	0.625	1.890	0.890	0.036
PSMS_BL	0.028	0.067	0.675	-0.233	0.098	0.020
CHARLSON	-0.058	0.511	0.910	-0.095	0.541	0.860
SCID_CURRMDD_BL	-1.400	1.135	0.220	-2.982	1.338	0.028
KIDS_BINNo kids	-0.879	0.687	0.203	-1.515	0.763	0.050
AGE_BL	-0.043	0.028	0.124	0.556	0.342	0.107
AGE_sq	0.000	0.000	0.103	-0.005	0.003	0.067
EMPLOY3: Employed part-time	-1.509	1.021	0.142	-1.503	1.095	0.173
EMPLOY3: Not employed	-1.293	0.633	0.043	-0.782	0.687	0.257
MENOSTATFINAL_BL: Peri-menopausal	-0.545	1.733	0.754	-2.624	1.906	0.171
MENOSTATFINAL_BL: Post-menopausal	-0.268	1.285	0.835	-1.979	1.355	0.147
MENOSTATFINAL_BL: Pre-menopausal	0.741	1.362	0.587	-0.613	1.709	0.721
RSES_BL	0.065	0.064	0.313	0.185	0.090	0.042

TABLE 3. Bivariate and multivariate regression output for the top model in TABLE 2.

CONCLUSION

In our final model, we find statistically significant positive relationships between CAR and education level, income level, and Rosenberg Self-Esteem Scale, and a statistically significant negative relationship between CAR and the Perlin-Schooler Mastery Scale. A statistically significant negative relationship between CAR and unemployment disappears after adjusting for other covariates, while self-esteem becomes significant.

DISCUSSION

Findings suggest that it is worthwhile to further investigate education, income, perceived mastery of one's own life, diagnosis of major depressive disorder, employment, and self-esteem as characteristics that might be indicative of a patient in need of targeted intervention before beginning adjuvant cancer treatment.

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