Assessing Key Factors Associated with Depression before Adjuvant Therapy in Women with Breast Cancer



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OBJECTIVE

- Assess the relationship between CES-D (Center for Epidemiological Studies Depression Scale) and biobehavioral risk variables in women with early-stage breast cancer before they receive adjuvant therapy.
- Identify which variables explain changes in CES-D in this population and which are interesting for further study and targeted intervention.

INTRODUCTION

- Depression, as quantified by the CES-D, is one of the most common and neglected side effects of cancer and its treatment. It will lead to negative consequences for patients, and may even affect treatment compliance and efficacy¹.
- CES-D is recognized as a very common measure for assessing depressive symptom in women during cancer treatment², but only a few studies examine biobehavioral factors associated with fatigue before treatment.

METHODS

- We analyzed data from the RISE study. Patients with stage 0 to stage IIIA were recruited before the onset of adjuvant or neoadjuvant therapy. 270 patients' data was available, among them 25 (9.3%) observations were excluded because of the missing value.
- We first used bivariate linear regression. Predictors with p-value
 0.1 were included in subsequent multivariate linear regression.
- Component-plus-residual plot was used to explore nonlinear relationship between age and CES-D score. The plot suggests using a quadratic specification for age.
- Residual plot and q-q plot were used to check if the assumptions of the model were met. Influence plot was used to detect observations with high residual and leverage.

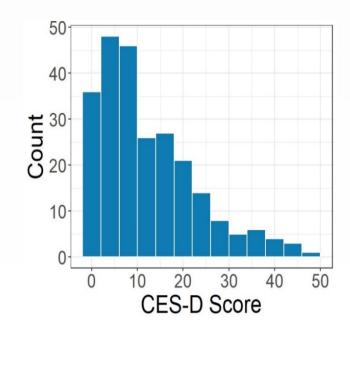
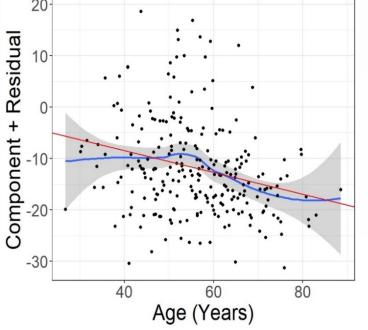
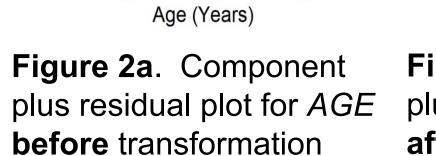


Figure 1. Histogram

of CES-D Score





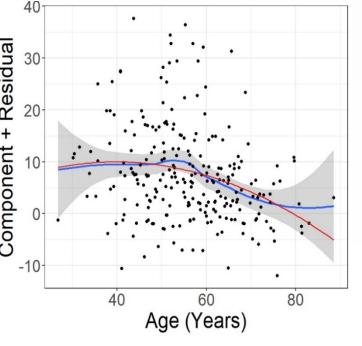


Figure 2b. Component plus residual plot for AGE after transformation

Table 1. Summary of Characteristics

Characteristics	Patients ¹ (N=245)	Characteristics	Patients ¹ (N=245)				
Demographics		Cancer stage at diagnosis					
Age (yr)	56.0 (11.3)	Stage 0	31 (13)				
Employment: yes	150 (61)	Stage 1	120 (49)				
Partnered status: yes	159 (66)	Stage 2	63 (26)				
Annual income		Stage 3 or higher	31 (13)				
< \$60,000	61 (25)	Biobehavioral risk factors					
\$60,000-\$100,000	47 (19)	Body mass index (kg/m²)	3.2 (0.2)				
≥ \$100,000	137 (56)	Charlson comorbidity index ²	0.3 (0.6)				
Education		History of depression: yes	56 (23)				
At most a high school degree	70 (29)	Leisure-time exercise					
College graduate	98 (40)	Often	92 (38)				
Post-graduate degree	77 (31)	Sometimes	90 (37)				
Race		Never/rarely	63 (26)				
White	175 (71)	Alcohol use					
Black	12 (5)	No drink	91 (37)				
Asian	29 (12)	Moderate drink	66 (27)				
Latino	6 (3)	Heavy drink	88 (36)				
Other	23 (9)	Childhood maltreatment					
Cancer stage and treatment		No maltreatment	150 (61)				
Breast cancer surgery		Non-sexual maltreatment	66 (27)				
Lumpectomy	142 (58)	Sexual maltreatment	29 (12)				
Mastectomy	80 (33)	 n (%); Mean (SE) A weighted index to predict risk of death wit 	hin 1-vear				

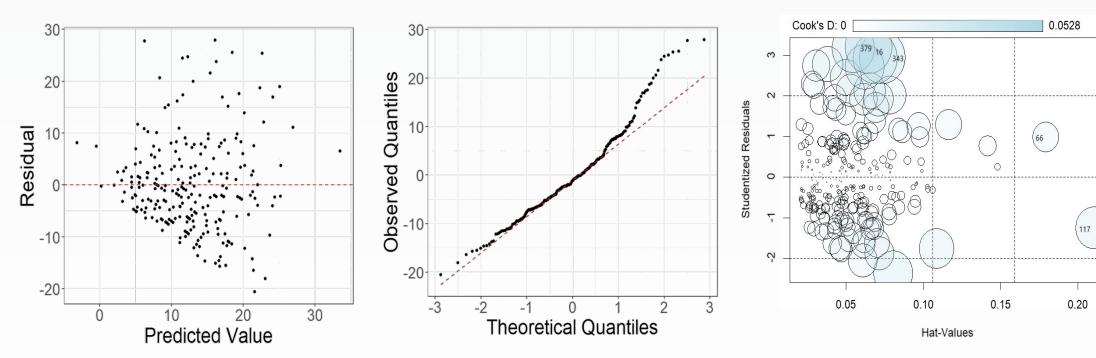


Figure 3. Residual plot

No surgery

Figure 4. Q-Q plot

Figure 5. Influence plot

- After bivariate regression, 7 variables are included in the multivariate regression. Figure 3 and Figure 4 are residual plot and q-q plot for Final Model. The variance of the residuals is slightly smaller when the predicted CES-D score is low. The residuals is not perfectly normal distributed because of the right skewness of CES-D.
- Figure 5 gives the influence plot for Final Model. Observations with high Cook's Distance are labeled with RISE ID. None of those observations were excluded in this study, but the outliers need attention.

RESULTS

 Table 2. Regression Results

Predictors	Bivariate Models		Multivariate Model (R ² =0.286)			Final Model (R²=0.296)		
	F-test P-value	t-test P-value	Coeff.	Std. Err	P-value	Coeff.	Std. Err	P-valı
Charlson comorbidity index	<0.01**	<0.01**	3.48	1.02	<0.01**	3.58	1.02	<0.01
Age (yr) Age Age square	<0.01**	<0.01** <0.01**	-0.21	0.05	<0.01**	0.50 -0.01	0.41 0.01	0.22 0.08
Annual income \$60,000-\$100,000 ≥ \$100,000	<0.01**	0.09 <0.01**	-2.33 -3.86	1.81 1.49	0.20 <mark>0.01**</mark>	-2.27 -3.91	1.81 1.48	0.21 <0.01
Breast cancer surgery Lumpectomy Mastectomy	<0.01**	0.58 0.01*	1.79 5.52	2.17 2.22	0.41 0.01*	1.42 5.09	2.17 2.22	0.51 0.02*
History of depression Yes	<0.01**	<0.01**	4.35	1.48	<0.01**	4.13	1.47	<0.01
Alcohol use Moderate drink Heavy drink	0.06	0.82 0.03*	-0.54 -2.30	1.51 1.40	0.72 0.10	-0.69 -2.46	1.51 1.40	0.65 0.08
Childhood maltreatment Non-sexual maltreatment Sexual maltreatment	<0.01**	<0.01** <0.01**	3.93 5.96	1.40 2.00	<0.01** <0.01**		1.40 1.00	<0.01 <0.01

DISCUSSION

- According to the final multivariate model with a quadratic specification for age, patients with higher annual income tend to have lower CES-D score. In addition, history of depression and childhood maltreatment experiences are related to higher CES-D score. Besides, patients that had a mastectomy and more medical comorbidities before enrollment in study have higher CES-D score after controlling for other variables.
- Because of the existence of heteroscedasticity, the standard errors may be biased. Other methods such as Weighted Least Squares should be conducted in further analysis.

CONCLUSION

Childhood trauma as well as past depression may have a profound effect on a person, and physicians need to pay close attention to the mental condition of breast cancer patients with these experiences. Mastectomy and medical comorbidities are not only physically taxing, but are also associated with depression. In addition to breast cancer treatment, such patients should be provided with timely psychological counseling.

FFFRFNCFS

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- 2. Hann D, Winter K, Jacobsen P. Measurement of depressive symptoms in cancer patients: evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *J Psychosom Res.* 1999;46(5):437-443. doi:10.1016/s0022-3999(99)00004-5