The Effect of Body Mass Index on Breast Cancer Stage and Breast Cancer-Specific Survival: A California Cancer Registry Study

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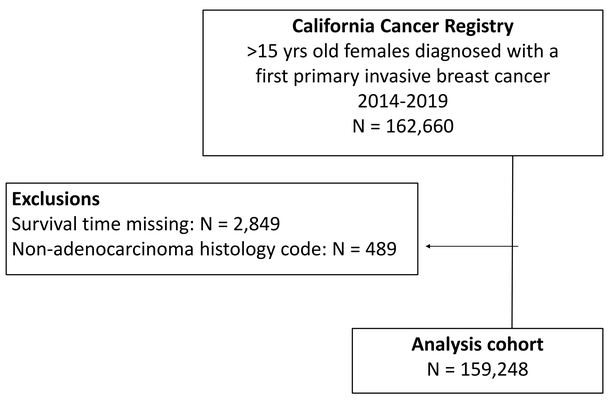
BACKGROUND

- Breast cancer (BC) is the most common and deadly malignancy worldwide.
- Obesity is on the rise globally, disproportionally affects women, and is a risk factor for the development, as well as recurrence, of BC depending on a women's age.
- Premenopausal women have an inverse relationship between weight and BC development versus postmenopausal women who are obese who have >2 times the risk of BC.
- Once diagnosed with BC, women with obesity of all ages have worse survival.
- Relationship between BMI and BC remains complex. How BMI is associated with stage of BC diagnosis and survival at various ages has not been well studied.
- Therefore, we used the population-based California Cancer Registry (CCR) to determine associations between BMI, BC stage at diagnosis, and BC- specific survival (BCSS).

Figure 1. Analysis cohort of AYAs with invasive primary breast cancers in California



METHODS

- 159,248 female patients (>15 years old) at diagnosis with invasive BC during 2014-2019 (**Figure 1**) were obtained from the CCR
- Body mass index (BMI) was calculated for each patient based on the formula: weight (kg)/height (m^2).
- Because of high proportion of missing BMI data (36.5%) multiple imputation by fully conditional specification methods were performed
- Multivariate logistic regression evaluated patient factors association with late stage of BC diagnosis. Late stage at diagnosis was defined as American Joint Committee on Cancer (AJCC) stage 3 and 4.
- Multivariable cox proportional hazard regressions (HR) models evaluated associations between BMI and other patient/clinical factors with BCSS.

Table 1. Late stage at Breast Cancer Diagnosis

	OR (95% CI)	P-value
Underweight (<18.5 kg/m^2)	**1.54 (1.5, 1.6)**	**p<0.0001**
Overweight (25-29.9 kg/m^2)	0.99 (0.9, 1)	p=0.11
Obesity class 1-2 (30-39.9 kg/m^2)	**1.06 (1.1, 1.2)**	**p<0.0001**
Obesity class 3 (>40 kg/m^2)	**1.14 (1.1, 1.2)**	**p<0.0001**

*As compared to patients who are normal BMI; multivariate logistic regression adjusted for other patient factors: race/ethnicity, age SES, health insurance, co-morbidities

Table 2. Breast Cancer Specific Survival Stratified by Age

	Age 15-39		Age 40-50		Age≥51	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Underweight (<18.5)	0.97 (0.6, 1.7)	p=0.91	**1.43 (1.0, 2.0)**	**p=0.045**	**1.18 (1.0, 1.4)**	**p=0.02**
Overweight (25-29.9)	1.14 (0.9, 1.4)	p=0.21	1.03 (0.9, 1.2)	p=0.68	0.95 (0.9, 1.0)	p=0.097
Obesity class 1-2 (30-39.9)	1.11 (0.9, 1.4)	p=0.38	1.05 (0.9, 1.2)	p=0.57	**0.93 (0.8, 0.9)**	**p=0.029**
Obesity class 3 (>40)	1.09 (0.74, 1.6)	p=0.67	1.17 (0.9, 1.5)	p=0.2	0.92 (0.8, 1.0)	p=0.11

*As compared to patients who are normal BMI; multivariate cox proportional hazards regression stratified by age adjusted for other factors: SES, insurance, tumor factors, treatment factors

RESULTS

- This cohort consisted of 34.5% of patients who had normal BMI, 53.3% non-Hispanic (nH) whites, 75.3% women ≥51 years old, and 39.8% women from the highest Socioeconomic Status (SES) neighborhoods.
- The majority had HR positive tumors (57.6%), ductal histology (72.5%), and AJCC stage 1 tumors (42.8%).
- Patients who were underweight, obesity class 1-2, and obesity class 3 were more likely to be diagnosed with late stage BC **(Table 1).**
- The association between BMI and BCSS varied by age (p<0.0001), so analyses were stratified by age group **(Table 2).**
- Underweight women aged 40-50 and ≥51 years experienced worse BCSS, while women who were obese (class 1-2) and ≥51 years experienced better BCSS **(Table 2).**
- Other factors significant for BCSS included:

  nH Black compared to nH White [HR 1.21, 1.13-1.29], ≥ 51 years old compared to age 15-39 [HR 1.17, 1.08-1.26], highest SES neighborhood compared to lowest [HR 0.81, 0.77-0.85], having public insurance compared to private [HR 1.26, 1.21-1.31], and BC subtypes HER2, TNBC, and TPBC compared to HR+ [HR 1.35, 1.25-1.46; HR 2.65, 2.51-2.8; HR 1.47, 1.36-1.58].
- The association of BMI and BCSS varied by stage (p<0.001); however, the stratified analysis showed BMI differences were not statistically significant for survival.

CONCLUSION

- We found that women with obesity were more likely to be diagnosed with late stage BC, which aligns with prior work showing women with obesity have more severe BC.
- Our findings of women who were underweight being more likely to be diagnosed at a late BC stage may relate to prior work showing decreased adherence to regular mammography screening.
- Patients who were underweight had worse BCSS in women ≥ 40 years indicating a high-risk group that should be assessed for sarcopenia and malnourishment when presenting for cancer treatment as these can affect efficacy of systemic therapy.
- Patients with obesity class 1-2 had improved BCSS in patients ≥ 51 years; potentially further evidence of the "obesity paradox" and that BMI is not the correct tool to assess metabolic health of patients.

This work was sponsored by the Doris Duke Charitable Foundation/Burroughs Welcome COVID-19 Fund and National Institute of Health, Building Interdisciplinary Research Careers in Women's Health at UC Davis through Grant Number: 5K12HD051958-19