Relationship Between Obesity and Triple-Negative Breast Cancer: A Retrospective Study

OAKLAND UNIVERSITY WILLIAM BEAUMONT

Mariam Aoun, B.S.[1], Anna Jahshan, B.S.[1], Nayana Dekhne, M.D.[2], Varna Taranikanti, M.D., Ph.D.[3]
[1]Oakland University William Beaumont School of Medicine, Rochester, Michigan
[2]Department of Breast Surgery, Beaumont Hospital, Royal Oak, Michigan
[3]Department of Foundational Medical Studies, Oakland University William Beaumont School of Medicine, Rochester, Michigan

Introduction

Breast cancer (BC) is the most prevalent cancer worldwide and is a commonly diagnosed malignancy in females in the US second to skin cancer.[1,2] BC is classified into four subtypes (Luminal A, Luminal B, HER2-positive and triple-negative) to provide clinical utility along with sufficient prognostic and predictive power. Of the four subtypes, the triple-negative breast cancer (TNBC) lacks expression of estrogen and progesterone receptors (ER, PR) along with the absence or faint expression of the human epidermal growth factor receptor-2 (HER-2). TNBC accounts for around 12-20% of all breast cancer cases.[10]

Several risk factors have been identified for breast cancer, such as increasing age, genetic mutations, exposure to radiation, lack of physical activity and exercise, alcohol consumption, smoking, hormone therapy, as well as being overweight or obese.[3,4,7,8,11] The exact relationship between obesity and breast cancer is not entirely clear. Numerous studies have shown that obesity is linked to tumor-promoting pathways, including insulin resistance and chronic inflammation. Adipose tissue also increases the levels of estrogen by excessive aromatization activity and may also induce oxidative stress that may facilitate the progression of tumors as well as their metastasis to other bodily tissues.[6,7]

Since TNBC patients present with poor prognosis and their association with body mass index (BMI) has not been studied, further research into how obesity may impact the prognosis of TNBC is highly warranted. TNBC has also consistently been shown to be more common in African-American women.[2] Therefore, stratifying the patient populations in each group by race/ethnicity may provide further insight.

Aims and Objectives

Aim I: Determine the relationship between BMI at diagnosis and triple-negative breast cancer prognostic factors.

Aim II: Study the association between obesity and TNBC patients with regard to demographic factors, including race, and ethnicity.

Methods

The study involved a retrospective review using data from Beaumont Hospital patient records. The recruitment of subjects will not be necessary, as this is a retrospective analysis. The enrollment of subjects for research data was obtained from the Beaumont Health System database through EPIC.

Inclusion criteria entailed adult female patients greater than 20 but younger than 80 years of age with evidence of breast cancer that received care at Beaumont Hospital. We focused specifically on patients who received breast-conserving therapy with radiation, and we included those who had at least a two-year follow-up after therapy. We limited the patient population to those with a clinical anatomic stage I, II, or III.

Variables of interest included weight, height, age, race/ethnicity, smoking and alcohol use, dates of diagnosis, follow-up, treatment, relapse (if applicable), and death (if applicable). Data on receptor status, BRCA1/BRCA2, family history, grade and stage, laterality, type of treatment, and response to treatment were also collected.

A statistical analysis was performed using a variety of statistical tests depending on the nature of the variable of interest. An unequal variance two-sample t-test, Chi-Square p-value, and Fisher Exact p-value were used in the study.

Results

Variables	BMI < 30	BMI > 30	p-value
Median Age	63.0	61.5	0.63
Initial Margin	Positive: 13% Negative: 39% Close: 48%	Positive: 9% Negative: 68% Close: 23%	0.076
Final Margin	Positive: 3% Negative: 79% Close: 18%	Positive: 0% Negative: 88% Close: 12%	0.66
T stage	Tis: 3% T1: 69% T2: 27% T3: 1.6%	Tis: 0% T1: 55% T2: 42% T3: 3%	0.33
N stage	N0: 88% N1: 11% N2: 1.5%	N0: 77% N1: 23% N2: 0%	0.26
Biopsy Grade	Grade 1: 10% Grade 2: 35% Grade 3: 55%	Grade 1: 5% Grade 2: 29% Grade 3: 67%	0.67
Race	White: 80% Black: 12% Other: 8%	White: 69% Black: 25% Other: 6%	0.24
Hypertension	Yes: 45% No: 55%	Yes: 66% No: 34%	0.052
Diabetes	Yes: 17% No: 83%	Yes: 75% No: 25%	0.35

There was no significant difference between the obese and non-obese groups with regard to prognostic factors in TNBC. There was also no significant difference between the two groups with respect to race/ethnicity (p-value < 0.05 was considered to be significant).

Conclusions

There was no association between BMI classification and prognosis of TNBC. There was also no significant difference between the obese and non-obese categories when considering demographic factors, including race and ethnicity. However, this study included a small sample size that met the inclusion criteria, and more studies are warranted to further investigate this relationship.

References

1. Chen, M. J., Wu, W. Y. Y., Yen, A. M. F., Fann, J. C. Y., Chen, S. L. S., Chiu, S. Y. H., … Chiou, S. T. (2016). Body mass index and breast cancer: Analysis of a nation-wide population-based prospective cohort study on 1 393 985 Taiwanese women. *International Journal of Obesity*, *40*(3), 524–530. https://doi.org/10.1038/ijo.2015.205

2. Sarkissyan, M., Wu, Y., & Vadgama, J. V. (2011). Obesity is associated with breast cancer in African-American women but not Hispanic women in South Los Angeles. *Cancer*, *117*(16), 3814–3823. https://doi.org/10.1002/cncr.25956

3. Engin, A. (2017). Obesity-associated breast cancer: Analysis of risk factors. In *Advances in Experimental Medicine and Biology* (Vol. 960, pp. 571–606). Springer New York LLC. https://doi.org/10.1007/978-3-319-48382-5_25

4. Gershuni, V., Li, Y. R., Williams, A. D., So, A., Steel, L., Carrigan, E., & Tchou, J. (2017). Breast cancer subtype distribution is different in normal weight, overweight, and obese women. *Breast Cancer Research and Treatment*, *163*(2), 375–381. https://doi.org/10.1007/s10549-017-4192-x

5. Chen, J. E., & Glover, G. H. (2016). HHS Public Access, Adult BMI change and Risk of Breast Cancer: National Health and Nutrition Examination Survey, *25*(3), 289–313. https://doi.org/10.1007/s11065-015-9294-9.

6. Li, H., Sun, X., Miller, E., Wang, Q., Tao, P., Liu, L., … Li, J. (2017). BMI, reproductive factors, and breast cancer molecular subtypes: A case-control study and meta-analysis. *Journal of Epidemiology*, *27*(4), 143–151. https://doi.org/10.1016/j.je.2016.05.002

7. Neuhouser, M. L., Aragaki, A. K., Prentice, R. L., Joann, E., Chlebowski, R., Carty, C. L., … Garnet, L. (2016). HHS Public Access, Overweight, Obesity and Postmenopausal Invasive Breast Cancer Risk *1*(5), 611–621. https://doi.org/10.1001/jamaoncol.2015.1546.

8. Morata-Tarifa, C., Valle-Goffin, J. J., Friedman, E. R., Picon-Ruiz, M., & Slingerland, J. M. (2017). Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA: A Cancer Journal for Clinicians*, *67*(5), 378–397. https://doi.org/10.3322/caac.21405

9. Harrigan, M., Ligibel, J. A., Bracken, M. B., Irwin, M. L., Playdon, M. C., & Sanft, T. B. (2015). Weight Gain After Breast Cancer Diagnosis and All-Cause Mortality: Systematic Review and Meta-Analysis. *Journal of the National Cancer Institute*, *107*(12), djv275. https://doi.org/10.1093/jnci/djv275

10. Turkoz, F. P., Solak, M., Petekkaya, I., Keskin, O., Kertmen, N., Sarici, F., … Altundag, K. (2013). The prognostic impact of obesity on molecular subtypes of breast cancer in premenopausal women. *Journal of B.U.ON.*, *18*(2), 335–341.

11. Yang, X. R., Chang-Claude, J., Goode, E. L., Couch, F. J., Nevanlinna, H., Milne, R. L., … Garcia-Closas, M. (2011). Associations of breast cancer risk factors with tumor subtypes: A pooled analysis from the breast cancer association consortium studies. *Journal of the National Cancer Institute*, *103*(3), 250–263. https://doi.org/10.1093/jnci/djq526

Acknowledgements

We would like to thank Jacob Keely for conducting the statistical analysis. We would also like to thank Kimberly Marvin and Dr. Joshua Dilworth for contributing to the data from the radiation oncology department.