Relationship Between Smoking and Triple-Negative Breast Cancer: A Retrospective Analysis

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Introduction

Breast cancer is the most common cancer in women in the United States and accounts for about 30% of all new cancers diagnosed in females each year.[1] It is also the second most common cause of cancer mortality. This alone goes to show the importance of continuous research in this field. About 10-20% of breast cancers are triple-negative breast cancers (TNBC).[2] They are characterized by the lack of expression of estrogen, progesterone and human epidermal growth factor. As a result, TNBC lacks a therapeutic target.

Some forms of TNBC are characterized by a wide range of mutations.[3] The molecular characteristics of each of these associated mutations vary, each presenting with a different histopathological change. TNBCs are poorly differentiated tumors, making diagnosis more difficult.[4] Hence, they are characterized by aggressive behavior with early metastasis to the central nervous system, bone, lung, and liver. Moreover, they have a short response period to available therapies, poor prognosis, high recurrence rate, and poor survival as compared to the other subtypes. [5, 6, 7] However, since the molecular characteristics vary significantly among the different types of TNBCs, the clinical and pathologic presentation play an important role in the prognosis. In addition, to get more insight into the etiology of TNBC, it is important to study other risk factors specifically associated with TNBC. An association between the African American population and TNBC has been established.[2] However, stratifying the group by smoking pack years has not yet been conducted.

Smoking is a lifestyle factor for many different health problems. Recently, tobacco smoke has shown to increase the risk of breast cancer in pre-menopausal women.[8] Cigarette smoke induces changes in epithelial cells.[9] Currently, there are no retrospective studies that look at the correlation between smoking and, specifically, TNBC. Hence, this research is undertaken to study the association of smoking with TNBC and its correlation with other prognostic factors associated with breast cancer.

Aims and Objectives

Aim I: Determine the relationship between smoking (pack years) at diagnosis and TNBC and other prognostic factors.

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

Methods

Study Design: The study is a retrospective chart review design using patients from the Beaumont Hospital's database through the EPIC system.

Inclusion Criteria: The study includes all patients with TNBC ages 20 through 80 who were diagnosed with TNBC within the past 10 years and who received breast conserving therapy with at least two years of follow-up. Both metastatic and non-metastatic TNBC subjects were included.

Exclusion Criteria: The study excluded all other types of breast cancer. Subjects over the age of 80 were not included in the study due to other morbid conditions that could play a role in the pathogenesis of cancer. Lastly, male subjects were not included.

Variables and Prognostic factors of Interest:
- Patient age
- Smoking and Alcohol Use
- Race/Ethnicity
- Year of diagnosis
- Laterality (the side of the body where the cancer originated)
- Grade and Stage
- Regional lymph nodes status
- Diagnostic and Staging
- Receptor Status
- BRCA1/2
- Surgery, Radiation Therapy type, location, and volume
- Chemotherapy/Immunotherapy

Results

Statistical Analysis: Statistical analysis was used to describe the characteristics of the patient sample and compare smokers with TNBC to non-smokers with TNBC and their association with other prognostic factors. Data was analyzed using SPSS software and statistical tests, including ANOVA, Chi-Square, and Fischer's Exact test, were used. P-values < 0.05 were considered significant.

	No Smoking (N = 47)	Smoking Pack Years <= 11.5 (N = 30)	Smoking Pack Years > 11.5 (N = 30)	P-value
Median Age	60	64.5	67	0.0104[1]
Diabetes	Yes: 21.3% No: 78.7%	Yes: 13.3% No: 86.7%	Yes: 20.7% No: 79.3%	0.6566[2]
Hypertension	Yes: 48.9% No: 51.1%	Yes: 46.7% No: 53.3%	Yes: 58.6% No: 41.4%	0.6128[2]
Initial Margin	Positive: 9.7% Negative: 45.2% Close: 45.2%	Positive: 14.3% Negative: 52.4% Close: 33.3%	Positive: 12.5% Negative: 54.2% Close: 33.3%	0.8918[3]
Final Margin	Positive: 4.8% Negative: 78.6% Close: 16.7%	Positive: 0.0% Negative: 80.8% Close: 19.2%	Positive: 0.0% Negative: 81.5% Close: 18.5%	0.8716[3]
T stage	T_{is}: 2.2% T_1: 63.0% T_2: 30.4% T_3: 4.3%	T_{is}: 3.4% T_1: 69.0% T_2: 27.6% T_3: 0.0%	T_{is}: 0.0% T_1: 62.1% T_2: 37.9% T_3: 0.0%	0.8477[3]
N stage	N_0: 82.6% N_1: 15.2% N_2: 2.2%	N_0: 86.2% N_1: 13.8% N_2: 0.0%	N_0: 90.0% N_1: 10.0% N_2: 0.0%	0.9458[3]
Biopsy Grade	Grade 1: 3.3% Grade 2: 33.3% Grade 3: 63.3%	Grade 1: 12.5% Grade 2: 16.7% Grade 3: 70.8%	Grade 1: 8.7% Grade 2: 43.5% Grade 3: 47.8%	0.2358[3]
Race	White: 63.0% Black: 19.6% Other: 17.4%	White: 90.0% Black: 10.0% Other: 0.0%	White: 83.3% Black: 16.7% Other: 0.0%	0.0112[3]

[1]ANOVA F-test p-value; [2]Chi-Square p-value; [3]Fisher Exact p-value

This study did not demonstrate an association between smoking status and prognostic factors of TNBC. There was also no significant difference between the two groups with regard to race/ethnicity.

Conclusions

In conclusion, our present study did not demonstrate an association between smoking status and prognosis of TNBC. This may be due to the small sample size of patients that met the inclusion criteria, leading to a limitation in the power of the study. However, given that TNBC is characterized by aggressive behavior with early metastasis, it is important that more studies with a greater number of patients are conducted.

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