TNBC vs Non-TNBC: A Retrospective Review of Differences in Mean Age, Family History, Smoking History, and Stage at Diagnosis

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Abstract: *Purpose:* This study was designed to compare mean age, ethnicity, smoking history, family history of breast cancer, and stage at diagnosis in patients with triple-negative breast cancer (TNBC) vs non-TNBC at an inner city university program. *Methods:* We reviewed data in our tumor registry on patients seen between January 2000 and December 2005, and identified a total of 445 patients with various subtypes of breast cancers. Of these, 342 patients met our study criteria. Thirty-nine patients had TNBC and 303 had non-TNBC. *Results:* The mean age at diagnosis was 59.87±15.67 years for TNBC and 60.09±13.98 years for non-TNBC (*P*=.9272). TNBC was more common in black than in white patients (58.97% vs 35.90%; OR, 2.755; *P*=.004), and non-TNBC was more common in white than in black patients (57.76% vs 39.27%). There was not a statistically significant difference in past or present smoking between the TNBC and non-TNBC patients (20.51% vs 27.72%; *P*=.4385). Family history of breast cancer was not statistically related to TNBC status: a positive family history was reported in 30.77% of TNBC patients vs 33.33% of non-TNBC patients (*P*=.8384), no family history was reported in 51.28% of TNBC patients vs 51.82% of non-TNBC patients, and family history was unknown in 17.95% of TNBC patients vs 14.85% of non-TNBC patients. Pathologic stage at the time of diagnosis was as follows for TNBC vs non-TNBC patients: stage 0, 15.79% vs 11.37% (*P*=.4332); stage I, 34.21% vs 30.98% (*P*=.6890); stage II, 28.98% vs 37.25% (*P*=.3205); stage III, 18.42% vs 17.25% (*P*=.8591); and stage IV, 3.63% vs 3.14% (*P*=.8651). *Conclusion:* We found that in our patient population, black women were significantly more likely to have TNBC than non-TNBC, and white women were more likely to have non-TNBC than TNBC.

Introduction

Breast cancer is one of the most common forms of cancer in women, representing approximately one-quarter of the 1.1 million malignancies newly diagnosed in women per year.[1,2] Breast cancer is also the leading cause of cancer-related deaths throughout the world,

Table. Comparison of Demographics and Clinicopathologic Characteristics in TNBC and Non-TNBC Patients

Possible Risk Factors		TNBC (n=39)	Non-TNBC (n=303)	
Mean age at diagnosis, years		59.87±15.67	60.09±13.98	*P*=.9272
Ethnicity	**Black**	58.97%	39.27%	OR, 2.755; *P*=.004[a]
	White	35.90%	57.76%	
	Asian	2.56%	0.99%	
	Other	2.57%	1.98%	
Smoking history (past or present)	**Yes**	20.51%[b]	27.72%[b]	*P*=.4385
	No	71.79%[b]	61.72%[b]	
Family history of breast cancer	**Yes**	30.77%	33.33%	*P*=.8384
	No	51.28%	51.82%	
	Unknown	17.95%	14.85%	
Stage at diagnosis	**Stage 0**	15.79%	11.37%	*P*=.4332
	Stage I	34.21%	30.98%	*P*=.6890
	Stage II	28.98%	37.25%	*P*=.3205
	Stage III	18.42%	17.25%	*P*=.8591
	Stage IV	3.63%	3.14%	*P*=.8651

OR, odds ratio; TNBC, triple-negative breast cancer.

[a] OR refers to odds of black vs white patients having TNBC.

[b] Numbers do not add up to 100% because data were missing for some patients.

with case fatality rates highest in developing countries.[3] Despite the increased educational and monetary investments by various public and private sector interest groups to improve outcomes, breast cancer remains the second most important cause of cancer-related mortality in the US population.[4] Per the 2002 National Cancer Control Programme guidelines set forth by the World Health Organization, early detection and adequate therapy have been singled out as the most important factors in the fight for reduction in breast cancer mortality.[5]

In recent years, breast cancer has been classified on the basis of estrogen receptor (ER) or progesterone receptor (PR) status, and whether the human epidermal growth factor 2 receptor (HER2/neu) protein is overexpressed. Breast cancer that is negative for ER, PR, and HER2/neu is considered to be triple-negative breast cancer (TNBC). This type of breast cancer is noted for its propensity to metastasize earlier and display a more aggressive course than its non-TNBC counterpart.

Methods

For this 5-year retrospective cohort study, we reviewed data from the tumor registry at the University of Florida at Jacksonville from January 2000 through December 2005. Charts were reviewed with particular attention to patient characteristics, including mean age at diagnosis, ethnicity, past or present smoking, family history of breast cancer, and stage at diagnosis. We identified a total of 445 patients with various subtypes of breast cancers. The analysis included only those patients in whom the status of ER, PR, and HER2/neu protein overexpression was recorded. Our selection criteria led to the exclusion of 103 patients. Of the remaining 342 patients, 39 had TNBC and 303 had non-TNBC.

Results

The mean age at diagnosis was 59.87±15.67 years for TNBC patients vs 60.09±13.98 years for non-TNBC patients (*P*=.9272). In terms of ethnicity, TNBC vs non-TNBC patients had the following racial backgrounds: black, 58.97% vs 39.27%; white, 35.90% vs 57.76%; Asian, 2.56% vs 0.99%; and other, 2.57% vs 1.98%. TNBC was more common in black than in white patients (58.97% vs 35.90%; OR, 2.755; *P*=.004). Regarding smoking in TNBC vs non-TNBC patients, there was a positive smoking history in 20.51% vs 27.72% of the patients (*P*=.4385) and no smoking history in 71.79% vs 61.72% of the patients. Regarding family history of breast cancer in TNBC vs non-TNBC patients, there was a positive family history of breast cancer in 30.77% vs 33.33% of patients (*P*=.8384), no family history in 51.28% vs 51.82% of patients, and an unknown family history in

17.95% vs 14.85% of patients. The pathologic stage at the time of diagnosis for TNBC vs non-TNBC patients was as follows: stage 0, 15.79% vs 11.37% (*P*=.4332); stage I, 34.21% vs 30.98% (*P*=.6890); stage II, 28.98% vs 37.25% (*P*=.3205); stage III, 18.42% vs 17.25% (*P*=.8591); and stage IV, 3.63% vs 3.14% (*P*=.8651). These findings are summarized in the table.

Discussion

The World Health Organization classifies breast cancer according to histopathologic characteristics.[6] While this method successfully separates breast cancer into several invasive subtypes, it fails to predict prognosis and does not provide information to guide the selection of targeted treatment options.[7] Recent advances in the techniques used for immunohistochemical and gene expression studies have led to a distinct subdivision of breast cancer on the basis of protein expression and molecular subtypes, respectively.[8-11] These newer techniques have resulted in the classification of breast cancer on the basis of expression of HER2/neu proteins and estrogen and progesterone receptors.[12] This classification scheme has led to the recognition of TNBC, which refers to breast cancer that lacks expression of estrogen and progesterone receptors and does not overexpress HER2/neu proteins.[13-15]

Owing to its unique pathologic and clinical features, including younger age at diagnosis, higher propensity for distant visceral metastasis, poor outcomes, and a more aggressive overall presentation, TNBC has recently become the focus of intense research.[16] The TNBC subtype generally carries a worse prognosis than its non-TNBC counterpart; however, it carries a much more favorable response to neoadjuvant and adjuvant chemotherapies.[17] TNBC has a higher predilection for certain ethnicities, which is why its incidence has ranged from 11.2% in studies with a predominantly white patient population to as high as 39% in studies with a larger proportion of black patients.[18,19] In the Western world, the prevalence of TNBC is considered to be approximately 15% to 20% of cases.[20,21] Based on our research, the prevalence of TNBC at our institution is 12.87%. While this percentage is lower than the generally agreed-upon frequency, we can attribute our lower prevalence to the diverse demographics in our sample population.

Another important prognostic factor is the median age of patients at the time of breast cancer diagnosis.[22] Differences exist in age at diagnosis for the various breast cancer subtypes. TNBCs tend to occur at an earlier age than non-TNBCs.[23] Because TNBC subtype has only recently been recognized as a distinct entity, it is not well understood whether the prognosis differs between patients who develop TNBC at a younger age vs those who develop it at an older age.[23] Similarly, the available research data are not conclusive enough to make a convincing argument for or against a biological or clinical difference in TNBC patients based on age at diagnosis.[23] The sparse research data available on breast cancer in general have shown variable results, with some making a strong case for age as a distinct prognostic factor in younger patients and others failing to support this relationship.[24,25] Our research study adds further statistical analysis to this growing body of evidence. We found that in our inner city university program, there was no difference in mean age at the time of diagnosis between TNBC and non-TNBC patients.

Breast cancer subtypes also have a strong association with certain ethnic backgrounds. Data pooled from several research studies have indicated that black women are more likely to have TNBC than white women.[26-31] At our inner city institute, we found a significant statistical difference between the various ethnicities and their rates of the 2 breast cancer subtypes. We found that TNBC was more prevalent in black women, whereas non-TNBC was more prevalent in white women.

Several in vivo and in vitro studies have shown that cigarette smoke has carcinogenic properties, and that breast tissue is a potential target for these carcinogens.[32] Although the mechanism of action is not entirely understood, it is believed that the carcinogens in cigarette smoke are transported by plasma lipoproteins from the alveoli to the breast tissue.[33,34] Because of cigarette smoke's strong affinity for these lipoproteins, it is more likely to be stored in adipocytes in the breast tissue, and later be activated by the human mammary epithelial cells to unleash its carcinogenic effect.[35] The number of cigarette smoke–based DNA adducts is significantly higher in smokers than in nonsmokers.[36-38] Furthermore, researchers point to the higher accumulation of *P53* gene mutations in breast cancer tumors of smokers than in those of nonsmokers, which is comparable to the mutational spectrum seen in lung cancer patients.[39]

In addition to the aforementioned biological explanations, cigarette smoke is thought to have an antiestrogenic effect. This is supported by the observation that smokers have lower bone density, earlier age at menopause, decreased urinary levels of estrogens, and an attenuated response to hormone therapy compared with nonsmokers.[40-43] Ironically, although cigarette smoke is considered a risk factor for breast cancer, it can also play a protective role against breast cancer owing to its antiestrogenic effect.[44] With both a detrimental as well as a beneficial profile, it is not difficult to imagine why several previously published research studies have shown inconsistent results about the relationship between cigarette smoking and breast cancer.[45] More recent research studies, however, have suggested a strong correlation between breast cancer and smoking in long-term cigarettes smokers and in those who smoked before the birth of their first child.[46-50] In our research, there

was no significant association between smoking status and breast cancer subtypes, which is in agreement with some of the earlier studies mentioned above.

In our research study, we also looked into family history and its relationship with TNBC and non-TNBC. About 10% of women with breast cancer have a positive family history of breast cancer.[51] A history of breast cancer in a first-degree relative increases the risk for breast cancer by as much as 2-fold.[51-53] Both breast and ovarian cancers in first-degree relatives are considered established risk factors for the development of breast cancer.[51,54] In addition to its prognostic significance, a positive family history is associated with improved adherence to early detection strategies, such as regular screening mammography.[55-58] Women with a positive family history are less likely to have false beliefs about breast cancer and more likely to receive early breast cancer screenings and comprehensive breast cancer treatment.[59,60] This might explain why we had a high prevalence of breast cancer patients with a positive family history of breast cancer. Published studies have noted elevated breast cancer mortality in women who have low participation rates in mammography screening programs.[61] This further underscores the importance of mammography and future implications for patients who have a family history of breast cancer. In our study, we found no significant association between a positive family history of breast cancer and TNBC vs non-TNBC subtypes. It is important to note that based on several published studies, a positive family history of breast cancer does not impact all-cause mortality.[62-71] Furthermore, *BRCA1* and *BRCA2* germline mutations account for only one-quarter of the total breast cancer cases, and a significant portion of women with breast cancer acquire the disease in the absence of this familial link.[72]

Stage at diagnosis likely plays the most significant role in breast cancer mortality. Published research data by the National Cancer Institute have shown that the 5-year survival rate among women diagnosed with breast cancer at stage I is as high as 88%, whereas those whose disease is diagnosed at stage IV have a survival rate of approximately 15%.[73,74] Non-Hispanic white and Asian women are more likely to be diagnosed at an early stage, whereas Hispanic and black women are likely to be diagnosed at an advanced stage.[73,74] In our retrospective cohort research study, when we accounted for stage at the time of diagnosis, TNBC was as prevalent as non-TNBC at all stages. We found no significant difference in the stage at diagnosis between TNBC and non-TNBC patients in our patient population.

Conclusion

Our findings further contribute to the growing body of evidence pertaining to the association of certain demographic and clinicopathologic characteristics with TNBC and non-TNBC. We found a statistically significant ethnic predisposition for these 2 subtypes of breast cancers in our patient population. Black women were more likely to have TNBC, whereas white women were more likely to have non-TNBC. We did not find a significant difference in mean age, cigarette smoking, family history of breast cancer, and stage at diagnosis between the TNBC and non-TNBC patients. These findings are consistent with those from previously published research studies.

Disclosures

The authors have declared no relevant conflicts of interest.

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