



Triple Negative Invasive Breast Cancer: Association with Low Body Mass Index and Race

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Abstract

Background: The triple negative immunophenotype (ER-/PR-/HER2-) constitutes 15% of all invasive breast cancers and is associated with a poor prognosis. This phenotype accounts for the vast majority of basal subtype breast cancers identified by expression profiling. We sought to define the clinical and pathologic features of the patients and their triple negative invasive breast tumors in a diverse population.

Material and Methods: We established a database from an ethnically and socio-economically diverse patient population receiving care at a tertiary facility that is the largest safety net hospital in New England, with IRB approval. We identified female invasive breast cancer patients diagnosed 1998 - 2006 for whom there was information at diagnosis on tumor grade, stage, ER/PR expression, HER2 status, patient age, BMI using standard NHLBI (National Heart, Lung and Blood Institute) cut offs, and self identified racial group. All tumors were assessed using IHC and image analysis. HER2 2+ tumors were further assessed by FISH. We used contingency tables and multivariate logistic regression to determine associations between patient and tumor characteristics.

Results: 364 cases were identified; they were racially diverse (34% white, 50% black, 10% Hispanic, and 6% other). Elevated BMI was common (1% underweight, 23% normal, 28% overweight, 29% obesity I, 12% obesity II, and 7% extremely obese). 73% were post-menopausal, 60% were ER+/PR+, 12% were HER2 over expressed/amplified, and 20% were triple negatives. The probability of triple negative tumors was associated with race/ethnicity ($p < 0.01$) and with lower BMI ($p = 0.02$). Mutually adjusting for race and BMI, the odds of triple negative tumors were 3 fold higher (95% CI 1.6, 5.6) in black women than in white women, and 0.54 fold lower (95% CI 0.16, 1.81) in obese women than in normal/underweight women. After adjusting for race/ethnicity, there was a significant decreasing trend in the proportion of triple negative tumors with increasing category of BMI ($p = 0.03$). The proportion of patients with triple negative tumors did not vary significantly with age. Our database also identified previously described correlations between: increasing patient age and hormone receptor status ($p = 0.05$), race and hormone receptor status ($p < 0.01$), and triple negative tumors and increased grade ($p < 0.01$).

Discussion: We report significant independent associations between triple negative invasive breast cancer and both race and lower BMI. Our findings suggest that triple negative tumors are more prevalent in particular racial/ethnic groups, who may have distinct genetic backgrounds; and they may be less dependent on estrogen exposure, presumably from peripheral conversion, for growth stimulation.

Methods

Characteristics of the Study Sample

CHARACTERISTICS	N	(%)
AGE		
20 to < 45	53	(14)
45 to < 55	94	(26)
55 to < 65	106	(29)
65 to < 75	65	(18)
75+	46	(13)
RACE		
White	124	(34)
Black	182	(50)
Hispanic	37	(10)
Other	21	(6)
BMI (kg/m²)		
Underweight	3	(1)
Normal	81	(23)
Overweight	99	(28)
Obesity I	102	(29)
Obesity II	44	(12)
Extreme Obesity	27	(7)
ER / PR STATUS		
ER+ PR+	216	(60)
ER+ PR-	38	(10)
ER- PR+	7	(2)
ER- PR-	100	(28)
HER 2 STATUS		
HER2 +	45	(12)
HER2 -	316	(88)
TRIPLE NEGATIVE		
Yes	71	(20)
No	288	(80)
AJCC T STAGE*		
T0 / T1 mic	3	(1)
T1a	16	(5)
T1b	45	(13)
T1c	126	(36)
T2	115	(33)
T3	27	(8)
T4	4	(1)

*16 cases with T stage not determined, many in the case of metastatic disease on present # on. F frequency missing 12

•We collected patient specific data by querying aggregated, electronic clinical data stored in an Oracle database. We performed manual medical review of the extracted data to ensure quality control.

•We identified 364 independent invasive breast tumors from 359 patients for whom we had information at diagnosis on tumor grade, stage, ER/PR expression, HER2 status, patient age, BMI using standard NHLBI cut offs, and racial groups.

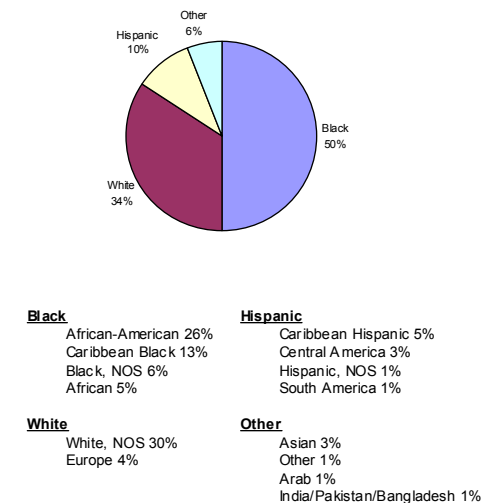
•All tumors were assessed via single institution pathology review using IHC and image analysis. HER2 2+ tumors were further assessed by FISH.

•Racial/ethnic groups were based on country of origin as reported on patient registration to the institution, and were confirmed by physician provider. The geographical diversity of the women in our study did not lend itself to the conventional racial/ethnic groupings used in the United States.

•BMI was determined as near as possible to cancer diagnosis within a window of 18 months – from 6 months pre diagnosis to 12 months post diagnosis. NHLBI cut offs in kg/m²: underweight <18.5, normal 18.5 – 24.9, overweight 25 – 29.9, obesity (class 1) 30 – 34.9, obesity (class 2) 35 – 39.9 and extreme obesity (class 3) > 40.

Results

Percentage Distribution of Tumors by Race/Ethnicity



•The cohort was racially diverse: 34% white, 50% black, 10% Hispanic, and 6% other. 73% were post-menopausal, and elevated BMI was common.

•Most were hormone receptor positive (ER+/PR+) 60%, 12% were HER2 over expressed/amplified, and 20% were triple negatives.

•The probability of triple negative tumors was associated with race/ethnicity ($p < 0.01$) and with lower BMI ($p = 0.02$).

•Mutually adjusting for race and BMI, the odds of triple negative tumors were 3-fold higher (95% CI 1.6, 5.6) in black women than in white women, and 0.54-fold lower (95% CI 0.16, 1.81) in obese women than in normal/underweight women.

•After adjusting for race/ethnicity, there was a significant decreasing trend in the proportion of triple negative tumors with increasing category of BMI ($p = 0.03$).

Conclusions

•We report significant independent associations between triple negative invasive breast cancer and both race and lower BMI.

•Our findings suggest that triple negative tumors are more prevalent in particular racial/ethnic groups, who may have distinct genetic backgrounds.

•Triple negative tumors may be less dependent on estrogen exposure, presumably from peripheral conversion, for growth stimulation.

•An understanding of the clinical and pathologic features of patients with the triple negative immunophenotype may act as a surrogate to understanding the basal-like subtype, help to anticipate poor risk tumors and institute the most active therapies.