Inflammatory Breast Cancer in a Population of Puerto Rican Women

Valeria Rullán-Varela[1]; Camiled Quirindongo-Rivera[2,3]; Karen J Ortiz-Ortiz[2,4]; Michelle Martínez-Montemayor[1]

[1]Universidad Central del Caribe-School of Medicine; [2]University of Puerto Rico Comprehensive Cancer Center; [3]Public Health Program, Ponce Health Sciences University; [4]Puerto Rico Central Cancer Registry

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michelle.martinez@uccaribe.edu

Abstract

Inflammatory breast cancer (IBC) is a highly aggressive form of breast cancer (BC). It accounts for 2-5% of all breast cancers but is responsible for 7%-10% of breast cancer mortality in the United States. The incidence of IBC in the Puerto Rican population is unknown. The objective of this study is to describe the patient profile and the clinicopathological characteristics of IBC tumors in the Puerto Rican population. To achieve this, we designed a retrospective study determined to be exempt by the UCC-IRB. We used the Puerto Rico Central Cancer Registry (PRCCR) database and complemented it with the PRCCR-Health Insurance Linkage Database (PRCCR-HILD) to identify cases of Puerto Rican women diagnosed with IBC from 2008 to 2018. We identified a total of 51 patients and studied variables such as age at diagnosis, staging variables, tumor receptor status, and overall survival (OS). Our results suggest that the Puerto Rican IBC patient population presents unique characteristics. The mean age at diagnosis of IBC in the current study was 59 years old, which is older than the mean age at diagnosis of IBC for women in mainland United States, but younger than the mean age women that are diagnosed with BC in PR (63 years old). Most tumors presented with ER+/PR+/Her2- (21.6%), or a triple negative (ER-/PR-/HER2-, 15.7%) tumor concordance, which is higher than the triple negative incidence in non-IBC BC Puerto Rican patients. The higher incidence of triple-negative IBC tumors within the Puerto Rican population resulted in poorer outcomes measured by a striking worse 3-year OS rate (36% [90% CI: 0.11-0.62]). Moreover, the most common tumor receptor subtypes were ER+/PR+ (39.2% [n=20]), and ER-/PR- (31.4% [n=16]). This study revealed through Cox regression analysis that patients with ER-/PR- tumor subtypes displayed a significantly higher risk of death (HR 4.83; [90% CI: 1.90-12.30]) than ER+/PR+ receptor subtypes. This is the first research to describe the epidemiology of IBC in Puerto Rico. In future studies, we will encourage physicians in Puerto Rico to report IBC cases to the PRCCR, and will disseminate diagnostic guidelines to increase awareness among clinicians and patients about this intractable disease.

Keywords: Inflammatory Breast Cancer; Molecular profile; Epidemiology; Puerto Rico Central Cancer Registry

Introduction

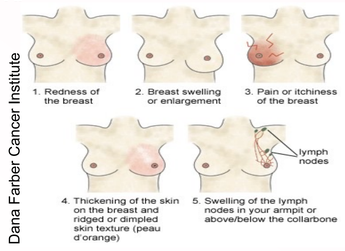
IBC is a highly aggressive form of BC (1,2). IBC is a rare and rapidly progressing BC subtype that is classically recognized by the appearance of edema, erythema, and pitting of the skin of the breast. In the United States (US), IBC accounts for 2-5% of all BC but is responsible for 7%-10% of BC mortality (1,2). The overall IBC 5-year survival is estimated at 40.5% (3). Despite this grim prognosis, the 5-year survival of patients with IBC has increased over time, probably due to multimodal treatment strategies that include neoadjuvant systemic therapy, followed by radiotherapy and surgery. Nevertheless, IBC's survival rate is still significantly lower than in non-IBC BC patients, which have an overall 5-year survival of 90.3% (4).

Per the American Joint Committee on Cancer (AJCC) TNM system, IBC tumors are designated as T4d at diagnosis (5). The diagnosis of IBC is clinicopathological since it must meet clinical criteria in addition to pathological confirmation of invasive carcinoma. The pathologic assessment of hormone receptors (ER and PR) and HER2/neu tumor receptor status is critical to the staging, the treatment plan, and possibly to the prognosis of the disease. Triple-negative and ER+/PR+/HER2- IBC tumors have been linked with poorer prognosis (6).

The characterization of IBC in Puerto Rican women has not been studied before. This study sheds light and describes IBC in the population of Puerto Rican women. Thus, the objective of the current study is to characterize the IBC Hispanic women population in Puerto Rico and estimate the IBC survival rate. Using the Puerto Rico Central Cancer Registry (PRCCR) database complemented with the PRCCR-Health Insurance Linkage Database (PRCCR-HILD), we aim to identify cases of Puerto Rican women diagnosed with IBC.

Data Collected

A.



B.

Data Collected
Tumor receptor status (ER, PR, HER2/neu) and tumor receptor concordance
Age at diagnosis
Staging variables
Survival Data
Age at death
Recurrence of IBC
Health Insurance
Marital status
Municipality
Type of treatment

Fig. 1. Signs and symptoms of IBC (A). Data collected as part of this study (B).

Methodologies

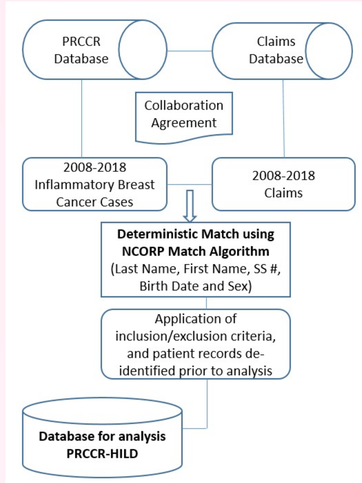


Fig. 2 SOP of patient recruitment and data collection. The study was done using the PRCCR database and data was complemented with PRCCR-Health Insurance Linkage Database (PRCCR-HILD). IBC patients were identified using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) site codes C50.0-C50.9 and histology code 8530.

Statistical Analysis

We used descriptive statistics and frequency analyses to describe the population of IBC patients in Puerto Rico. The Kaplan-Meier method was used to estimate survival curves and the log-rank test to assess differences between survival curves. We used Cox proportional hazards model to examine the effect of demographics and clinical variables on the risk of dying using the hazard ratios (HRs) with 90% confidence intervals (90% CIs). All analyses were performed using STATA version 17.0.

Results

Table 1. Demographic data of IBC patients	
Variables	**Number of patients**
Age at diagnosis	
<45	8
45-64	25
>65	18
Marital status	
Unmarried	30
Married	21
Treatment delay (days)	
<15	7
15-44	21
≥45	13
Health Insurance	
Medicaid and Medicaid-Medicare	26
Medicare	13
Private	12

Table 1. Epidemiological data collected of 51 IBC patients from the PRCCR database and the PRCCR-Health Insurance Linkage Database.

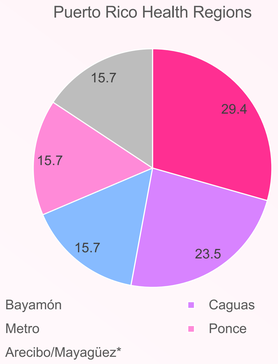


Fig. 3 Puerto Rico Health Regions. The Department of Health in Puerto Rico is segregated in seven health regions: Arecibo, Bayamón, Caguas, Fajardo, Mayagüez, Metro, and Ponce (7). No cases were reported in the Fajardo health region, which comprises the Rio Grande, Luquillo, Fajardo, Ceiba, Vieques, and Culebra municipalities.

Table 2. Tumor Receptor Concordance		
Tumor receptor concordance (ER/PR/Her2)	**Number of Patients**	**Percentage (%)**
ER-/PR-/Her2-	8	15.7
ER+/PR+/Her2-	11	21.6
ER-/PR-/Her2+	6	11.8
Not done*	11	21.6
Other**	15	29.4

Table 2. We identified the specific signatures that were expressed by all of the subjects: ER+PR+HER2/neu- (21.6%); ER-PR-HER2/neu- (15.7%); and ER-/PR-/Her2+ (11.8%). If the patient died before the test could be performed, it is listed as not done. Other refers to additional concordance subtypes.

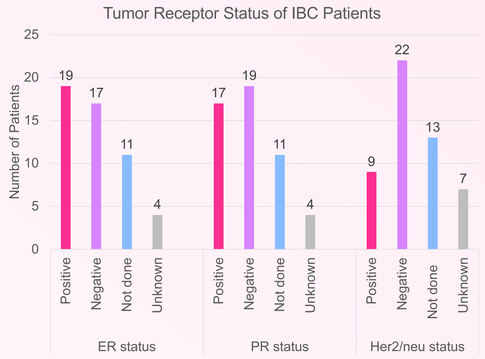


Fig. 4 Tumor Receptor Status of IBC Patients. The tumor receptor status of each subject was analyzed. (A) 19 of 51 subjects were positive for ER (37%),a 17 were positive for PR (33%) and 9 were positive for HER2/neu (18%).

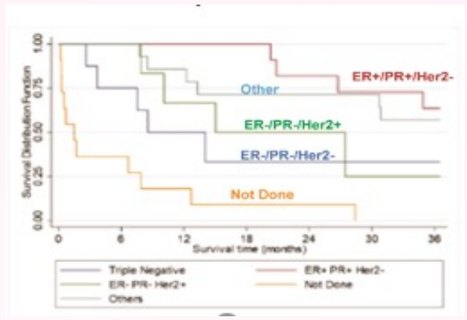


Fig. 5 Overall survival per tumor concordance. Triple negative subtype had worse survival at 36 months (36% [90% CI: 0.11-0.62]).

Discussion and Conclusion

- Our results suggest that the Puerto Rican IBC patient population presents unique characteristics.
- The mean age at diagnosis was 59 years old. Our results show that women in Puerto Rico were diagnosed with IBC at a slightly older age during this reported period. Women in Puerto Rico diagnosed with IBC were younger than those diagnosed with non-IBC BC, who are typically diagnosed at 60.5 years (8).
- The current study in Puerto Rican women found that 39.2% of IBC patients had ER+/PR+ tumors, while 31.4% of IBC patient tumors were classified as ER-/PR-. Our study revealed that patients with ER-/PR- tumor subtypes displayed a significantly higher risk of death (HR 4.74; [90% CI: 1.88-11.95]) than IBC patients with ER+/PR+ tumor receptor subtypes.
- In the general population of non-IBC BC in Puerto Rico, triple-negative tumors account for 9.5% of cases (11). Importantly, in our study, an alarming 15.7% of IBC patients presented with triple-negative disease (ER-/PR-/Her2-). The higher incidence of triple-negative IBC tumors within the Puerto Rican population results in poorer outcomes measured by a striking worse 3-year OS rate (36% [90% CI: 0.11-0.62]).
- The average delay in treatment for patients in our study was 15-44 days. Patients for whom treatment was delayed <15 days had a 6.69 higher risk of dying (HR 6.69; [90% CI: 1.16-38.73]) than patients with a delay in treatment ≥45 days, who had a 4.48 risk of death (HR 4.48 [90% CI: 1.10-18.23]).

- Limitations of this study include the lack of available information due to the low incidence of IBC in Puerto Rico and the possible clinical underreporting and misclassification of cases.

- In future studies, we aim to increase awareness among clinicians and patients about the signs and symptoms of this intractable disease. We will encourage physicians in Puerto Rico to report IBC cases to the PRCCR and also disseminate diagnostic guidelines to ensure an improved strategy for early detection of this devastating disease.

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