Sex-Based Differences in Hormone Receptor-Positive Breast Cancer Treatment and Outcomes: A Veterans Health Administration 20-Year Cohort Study

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Background:

- ER+ breast cancer is the most diagnosed subtype in both male and female patients
- Due to the rarity of male breast cancer (maleBC), there remains limited data of treatment and how outcomes compare between sexes

Objective:

- Compare **survival and treatment** for ER+ maleBC and female breast cancer (femBC) patients within the Veterans Health Administration (VHA)

Methods:

- Conducted a retrospective cohort study of patients diagnosed and treated with **ER+ maleBC and femBC between 2000-2020** using national VHA data
- Demographics, tumor characteristics, treatment, and survival were compared between maleBC and femBC
- Stage 0 and IV were excluded from our analysis
- Descriptive statistics, t-tests, and chi-square tests were used to compare the cohorts
- Cox proportional hazards regression models were used to estimate overall survival (OS) controlling for age, race, BMI, and grade

Demographic and Clinical Characteristics	Overall (n=6336)	Female (n=5202)	Male (n=1134)	P-value
Age at diagnosis, mean(SD)	59.75 (11.95)	57.74 (11.31)	68.97 (10.36)	<0.001
Race				
White	4194 (66.2)	3440 (66.1)	754 (66.5)	
Black	1474 (23.3)	1217 (23.4)	257 (22.7)	
Other/Unknown	668 (10.5)	545 (10.5)	123 (10.8)	0.838
Ethnicity				
Hispanic or Latino	293 (4.6)	250 (4.8)	43 (3.8)	
Not Hispanic or Latino	5774 (91.1)	4750 (91.3)	1024 (90.3)	
Unknown	269 (4.2)	202 (3.9)	67 (5.9)	0.004
Body mass index, mean(SD)	30.88 (9.36)	30.93 (9.80)	30.62 (6.98)	0.307
Histology				
Ductal	5271 (83.2)	4284 (82.4)	987 (87.0)	
Lobular	525 (8.3)	511 (9.8)	14 (1.2)	
Other/Unknown	540 (8.5)	407 (7.9)	133 (11.7)	<0.001
Grade				
I	1095 (17.3)	960 (18.5)	135 (11.9)	
II	2128 (33.6)	1683 (32.4)	445 (39.2)	
III	1171 (18.5)	900 (17.3)	271 (23.9)	
Unknown	1912 (30.2)	1633 (31.4)	279 (24.6)	<0.001

Table 1: Cohort demographics and tumor characteristics.

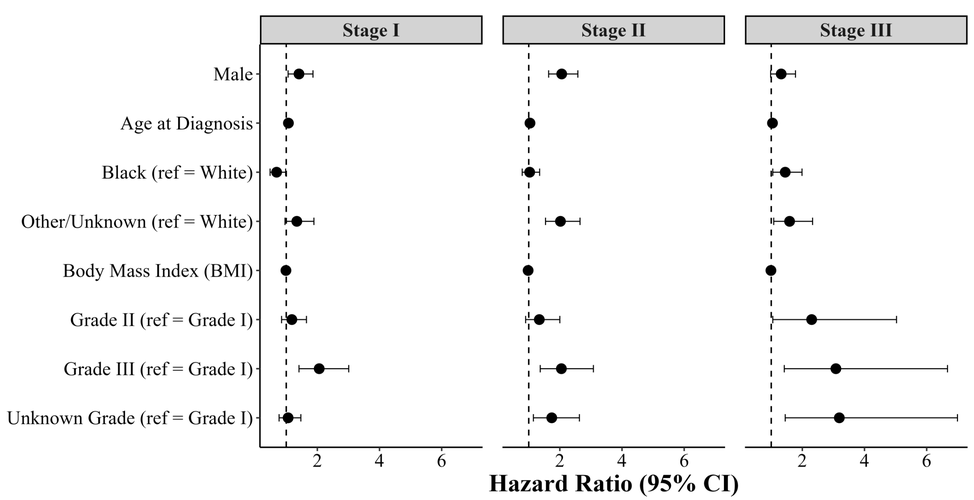


Figure 1: Forest plot of adjusted hazard ratios of all-cause mortality, stratified by stage.

Results:

- 6,336 patients met inclusion criteria, **17.9% (n=1,134) were male**
- ER+ maleBC patients were **significantly more likely** to:
  - be diagnosed at an older age (maleBC 69.0 vs. femBC 57.7 years; p <0.001)
  - present with higher stage disease (II: 46.5% vs. 33.2%; p<0.001, III: 20.9% vs. 10.1%; p <0.001)
  - Have ductal histology (87.0% vs. 82.0%); p<0.001)
  - Be diagnosed with higher grade disease (grade 2: 39.0% vs. 32.0%; p<0.001, grade 3: 24.0% vs. 17.0%; p<0.001)
- Compared to ER+ FBC patients, ER+ maleBC patients had **similar rates** of surgery and chemotherapy and **lower rates** of radiation (23.0% vs. 53.0%; p<0.001).
- In a Cox proportional model, ER+ stage I (aHR 1.41; 95% CI 1.06-1.86) and stage II MBC patients (aHR 2.06; 95% CI 1.64-2.58) had **significantly higher risk-adjusted hazard of overall mortality**

Conclusions:

- Despite receiving similar surgical and chemotherapy, ER+ maleBC patients were more often diagnosed at later stages and had significantly worse risk-adjusted overall survival compared to ER+ femBC
- Our findings highlight the need for increased awareness, earlier detection, and tailored treatment for ER+ maleBC

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