

# Breast Cancer Biology, Stage of Presentation, and Treatment in the Extremes of Age

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## Introduction

- Breast cancer = most common cause cancer-related deaths in women < 40y<sup>1</sup>
- Breast cancer = most common cancer in elderly women<sup>1</sup>
- Young women → more aggressive disease & treatment, ?worse survival<sup>2,3</sup>
- De-escalation of therapy endorsed in older women
- Paucity of data directly comparing young and elderly with breast cancer*

## Objective

To compare contemporary biology, stage of presentation, patterns of care, and overall survival in breast cancer patients at the extremes of age.

## Methods

- Adult patients, stages 0-IV breast cancer from 2004-2015 in the National Cancer Database
- Patients categorized by age:
  - 18-45y
  - 46-74y
  - ≥75y
- Patient characteristics compared
  - Chi-square and t-tests, as appropriate
- Survival analyses
  - Kaplan-Meier curves to visualize unadjusted overall survival
  - Cox proportional hazards model to estimate the effect of age group, after adjustment for known covariates
- Subset analysis of patients diagnosed in 2010 or later, to allow for adjustment of tumor biology (hormone-receptor [HR]+/HER2-, HER2+, triple-negative [TN])

## Results

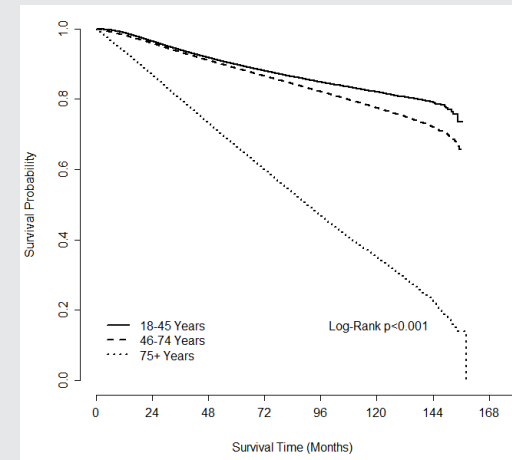
**Table 1. Patient and tumor characteristics.**

	All Patients (N=1,201,252)	Ages 18-45y (N=156,240)	Ages 75y+ (N=210,095)	P-value
<b>Histology</b>				<0.001
Ductal	880010 (73.3%)	122889 (78.7%)	147029 (70%)	
Lobular	233400 (19.4%)	22978 (14.7%)	45108 (21.5%)	
Other	87842 (7.3%)	10373 (6.6%)	17958 (8.5%)	
<b>Tumor Type</b>				<0.001
DCIS	169773 (14.1%)	20961 (13.4%)	22263 (10.6%)	
Invasive Non-Metastatic	989079 (82.3%)	129095 (82.6%)	180196 (85.8%)	
Invasive Metastatic	42400 (3.5%)	6184 (4%)	7636 (3.6%)	
<b>Clinical T Stage</b>				<0.001
T0/IS	192356 (16%)	24558 (15.7%)	25151 (12%)	
T1	631855 (52.6%)	63885 (40.9%)	120054 (57.1%)	
T2	276529 (23%)	48677 (31.2%)	47759 (22.7%)	
T3	54940 (4.6%)	12914 (8.3%)	7320 (3.5%)	
T4	45572 (3.8%)	6206 (4%)	9811 (4.7%)	
<b>Clinical N Stage</b>				<0.001
N0	1004429 (83.6%)	115957 (74.2%)	184318 (87.7%)	
N1	146788 (12.2%)	30770 (19.7%)	18989 (9%)	
N2	31886 (2.7%)	5973 (3.8%)	4701 (2.2%)	
N3	18149 (1.5%)	3540 (2.3%)	2087 (1%)	
<b>Clinical M Stage</b>				<0.001
M0	1161206 (96.7%)	150439 (96.3%)	202831 (96.5%)	
M1	40046 (3.3%)	5801 (3.7%)	7264 (3.5%)	
<b>Pathologic T Stage</b>				<0.001
T0/IS	154529 (12.9%)	23077 (14.8%)	18163 (8.6%)	
T1	535254 (44.6%)	57388 (36.7%)	97130 (46.2%)	
T2	224479 (18.7%)	34172 (21.9%)	41640 (19.8%)	
T3	35426 (2.9%)	6518 (4.2%)	5823 (2.8%)	
T4	16365 (1.4%)	1823 (1.2%)	4756 (2.3%)	
TX	203595 (16.9%)	29493 (18.9%)	34525 (16.4%)	
<b>Pathologic N Stage</b>				<0.001
N0	650012 (54.1%)	76447 (48.9%)	108733 (51.8%)	
N1	165391 (13.8%)	28705 (18.4%)	22142 (10.5%)	
N2	49743 (4.1%)	9309 (6%)	6879 (3.3%)	
N3	25057 (2.1%)	4132 (2.6%)	3662 (1.7%)	
NX	267390 (22.3%)	33055 (21.2%)	57302 (27.3%)	
<b>Pathologic M Stage</b>				<0.001
M0	747034 (62.2%)	90913 (58.2%)	127894 (60.9%)	
M1	12485 (1%)	2172 (1.4%)	1779 (0.8%)	
MX	441733 (36.8%)	63155 (40.4%)	80422 (38.3%)	
<b>Grade</b>				<0.001
1	258029 (21.5%)	19825 (12.7%)	54390 (25.9%)	
2	522699 (43.5%)	60558 (38.8%)	98974 (47.1%)	
3	420524 (35%)	75857 (48.6%)	56731 (27%)	
<b>ER Status</b>				<0.001
ER+	976250 (81.3%)	116531 (74.6%)	179920 (85.6%)	
ER-	225002 (18.7%)	39709 (25.4%)	30175 (14.4%)	
<b>PR Status</b>				<0.001
PR+	854346 (71.1%)	106235 (68%)	154745 (73.7%)	
PR-	346906 (28.9%)	50005 (32%)	55350 (26.3%)	
<b>HER2 Status (2010 &amp; after)</b>				<0.001
HER2+	95049 (12.6%)	17104 (18.6%)	11891 (9.2%)	
HER2-	540847 (71.7%)	60976 (66.2%)	99793 (77.5%)	
<b>Tumor Biology (2010 &amp; after)</b>				<0.001
HR+/HER2-	463374 (61.4%)	47241 (51.3%)	89285 (69.3%)	
HER2+	95049 (12.6%)	17104 (18.6%)	11891 (9.2%)	
TNBC	77473 (10.3%)	13735 (14.9%)	10508 (8.2%)	

\*ER: estrogen receptor. PR: progesterone receptor. HER2: human-epidermal-growth-factor-receptor-2. HR: hormone receptor. TNBC: triple negative breast cancer

**Table 2. Treatment characteristics.**

	All Patients (N=1201252)	Ages 18-45y (N=156240)	Ages 75y+ (N=210095)	P-value
<b>Surgery Type</b>				<0.001
Mastectomy	476583 (39.7%)	87566 (56%)	71444 (34%)	
Lumpectomy	661828 (55.1%)	61367 (39.3%)	120029 (57.1%)	
Other	913 (0.1%)	140 (0.1%)	122 (0.1%)	
No Surgery	61928 (5.2%)	7167 (4.6%)	18500 (8.8%)	
<b>Treatment with Chemotherapy</b>				<0.001
No	738269 (61.5%)	53512 (34.2%)	188703 (89.8%)	
Yes	462983 (38.5%)	102728 (65.8%)	21392 (10.2%)	
<b>Treatment with Radiation</b>				<0.001
No	515008 (42.9%)	68431 (43.8%)	127040 (60.5%)	
Yes	686244 (57.1%)	87809 (56.2%)	83055 (39.5%)	
<b>Treatment with Endocrine</b>				<0.001
No	452132 (37.6%)	64627 (41.4%)	91471 (43.5%)	
Yes	749120 (62.4%)	91613 (58.6%)	118624 (56.5%)	



**Figure 1. Unadjusted overall survival by age group.**

**Table 3. Unadjusted overall survival by age.**

Age	Total	Deaths	5-Year Survival Rate (95% CI)	10-Year Survival Rate (95% CI)
18-46	156240	16007 (10.2%)	0.898 (0.897-0.900)	0.821 (0.817-0.824)
47-74	834917	95849 (11.5%)	0.887 (0.886-0.888)	0.775 (0.773-0.777)
75+	210095	72832 (34.7%)	0.666 (0.663-0.668)	0.351 (0.346-0.356)
Total	1201252	184688 (15.4%)	0.850 (0.849-0.851)	0.705 (0.703-0.707)

**Table 4. Adjusted overall survival by diagnosis.**

	Hazard Ratio (95% CI)	P-Value	Overall P-Value
<b>DCIS (N=158,241)</b>			
Age Group			<0.001
18-45	REF		
46-74	2.187 (1.928-2.48)	<0.001	
75+	7.191 (6.28-8.235)	<0.001	
<b>Invasive, non-metastatic (N=915,994)</b>			
Age Group			<0.001
18-45	REF		
46-74	1.207 (1.179-1.237)	<0.001	
75+	3.057 (2.965-3.151)	<0.001	
<b>Invasive, metastatic (N=38,813)</b>			
Age Group			<0.001
18-45	REF		
46-74	1.166 (1.117-1.218)	<0.001	
75+	1.566 (1.479-1.659)	<0.001	

\*All models adjusted for year of diagnosis, gender, race/ethnicity, insurance status, income level, education level, facility type, facility location, distance traveled, Charlson/Deyo Comorbidity Score, histology, tumor grade, clinical T stage, clinical N stage, ER status, PR status, surgery type, radiation therapy, chemotherapy, and endocrine therapy.

## Data Highlights

1,201,252 patients → 13% ≤45y & 17.5% ≥75y

### Tumor Biology

- Grade 3 disease: younger > older
- HR+/HER2-: younger < older
- HER2+ & TN: younger > older

### Stage of Presentation

- cN0: younger < older
- De novo cM1: younger = older

### Patterns of Care

- Mastectomy, chemotherapy, & radiation: younger > older
- Endocrine therapy: younger > older

### Survival Trends

- Unadjusted OS: younger > older
- After adjustment, OS for all diagnoses: younger > older
- Association weakened with increasing disease severity

## Conclusions

- Significant differences in tumor biology & treatment between young & elderly patients with breast cancer
- Elderly women similarly at risk for incurable metastatic disease as younger women
- Thoughtful screening & treatment critical to prevent age-related disparities in care and outcomes

## References

- American Cancer Society: Breast Cancer Facts & Figures 2017-2018. Accessed 4/23/18
- Rosenberg SM, et al. Breast. 2015; 24 Suppl2:S154-158.
- Azim HA et al. BCR. 2014; 16(4):609-618.