Mortality Among Women Diagnosed With Stage II or III Breast Cancer Based on SEER-Medicare Data

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BACKGROUND

- Breast cancer is the most common malignancy and the second most common cause of cancer-related death among women in the United States (US).[1] American women have a 3% chance of dying from breast cancer, and in 2013, nearly 40,000 breast cancer-related deaths were expected nationally.[2]
- Nonmetastatic breast cancers include American Joint Committee on Cancer (AJCC) stages 0 (carcinoma *in situ*), I, II and III, and exhibit diverse histologic subtypes and clinical behaviors.[3] Systemic neo-adjuvant and adjuvant therapies, undertaken before and after surgery respectively, include cytotoxic chemotherapy, biologic therapy, and, depending on the patient's hormonal status, endocrine therapy.[4]
- These therapies increase disease-free survival by lowering the risk of recurrence and seeding from cancer cells that migrate from the primary tumor and their use is considered the current standard of care for stage II – III breast tumors.[5-8]
- Recent increased emphasis on assessing the quality of treatment (tx) for cancer patients has highlighted the need for real-world data sets that can address critical policy questions about cancer care in the US.
- This study examined treatment and mortality in women with incident early-stage breast cancer 2007–2009 using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data.

METHODS

- The SEER-Medicare linked database is developed by the US National Cancer Institute (NCI) and the Center for Medicare & Medicaid Services (CMS). The NCI-sponsored SEER program includes population-based tumor registries that routinely collect information on all newly diagnosed cancer (incident) cases in SEER areas, representing 28% of the US population.
- From the SEER-Medicare database, we identified women age >65 years at the diagnosis of breast cancer between 2007–2009, who received surgery and were enrolled with Medicare Parts A and B.
- To ensure a homogeneous sample of women treated with neoadjuvant or adjuvant chemotherapies, the cohort was limited to women diagnosed with AJCC stage II or III breast cancer because women with stage I disease are not always candidates for chemotherapies.[8]
- Women were followed from definitive surgery until the end of 2010, death, or change in enrollment status.
- Risk (cumulative incidence proportion [CIP]) of all-cause death was calculated with 95% confidence intervals (CI) using the Kaplan-Meier method stratified by tumor characteristics and treatment type.

RESULTS

- The cohort included 10,048 women with stage II (78%) or III (22%); 58% were ≥75 years and 78% had hormone-receptor (HR) positive tumors (77% ER positive, 64% PR positive). See Table 1a and b for descriptive characteristics.
- After the definitive surgery, 1,271 deaths reflected a CIP of 5.7% (95% CI 5.3–6.2) at 1 year, 10.9% (10.2–11.5) at 2 years, and 16.9% (15.9–17.9) at 3 years.

Table 1a. Demographics, Tumor Characteristics, and Treatment in Elderly Women Diagnosed With Breast Cancer Stages II/III in 2007–2009 and Treated With Surgery (N = 10,048)

Characteristic	N	%
Age at Dx.		
66–69	1705	17.0
70–74	2470	24.6
75–79	2233	22.2
80–84	1825	18.2
≥85	1815	18.1
Year of Dx.		
2007	3318	33.0
2008	3344	33.3
2009	3386	33.7
AJCC stage		
II	7859	78.2
III	2189	21.8
Size, cm		
≤2	2286	22.8
>2 – ≤5	6592	65.6
>5	1076	10.7
Unknown	94	0.9
Positive lymph node		
Negative	3755	37.4
Positive	5453	54.3
Unknown	840	8.4
Grade		
Well	1556	15.5
Moderately	4412	43.9
Poorly	3573	35.6
Undifferentiated	73	0.7
Unknown	434	4.3
Histology		
Ductal	6990	69.6
Lobular	1331	13.2
Mixed	1146	11.4
Unknown	581	5.8
ER/PR status		
ER+ and/or PR+	7843	78.1
ER- and PR-	1759	17.5
Unknown	446	4.4
Received trastuzumab (a surrogate for HER2-positive status)	715	7.1
Definitive surgery type		
Breast-conserving surgery	4310	42.9
Mastectomy	5738	57.1
Neoadjuvant Therapy		
Chemotherapy	557	5.5
Trastuzumab	112	1.1
Adjuvant Therapy		
Chemotherapy	3236	32.3
Trastuzumab	697	6.9

Table 1b. Baseline Comorbidities in Elderly Women Diagnosed With Breast Cancer Stages II/III in 2007–2009 and Treated With Surgery (N = 10,048)

Characteristic	N	%
Comorbid conditionsb		
ASHD	1480	14.7
CHF	844	8.4
CVA/TIA	799	8.0
Dysrhythmia	1432	14.3
PVD	1092	10.9
Cardiac disease, other	1217	12.1
Anemia	1415	14.1
CKD	634	6.3
COPD	1106	11.0
Dementia	505	5.0
Diabetes	2488	24.8
Diffuse connective tissue disease	67	0.7
GI disorder	260	2.6
Hypertension	6344	63.1
Liver disease	97	1.0
Osteoarthritis	1904	18.9
Osteoporosis	908	9.0
Rheumatoid arthritis	170	1.7

ASHD = arteriosclerotic heart disease; CHF = congestive heart failure; CVA/TIA = cerebral vascular accident / transient ischemic attack; PVD = peripheral vascular disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease

- Unadjusted mortality (Table 2) was higher among women with lymph node positive disease, women with neo-adjuvant tx, and those identified as "triple negative" phenotype (HR negative, no trastuzumab).

Table 2. Risk of Mortality (Cumulative Incidence Proportion), Overall and Stratified by Patient Characteristics

	Number at risk	Number of deaths	CIP (%)		
			1-year	2-year	3-year
All	10048	1271	5.7 (5.3, 6.2)	10.9 (10.2, 11.5)	16.9 (15.9, 17.9)
Age at diagnosis					
66–74	4175	248	2.9 (2.4, 3.5)	5.1 (4.4, 5.9)	8.1 (7.1, 9.3)
≥75	5873	1023	7.7 (7.1, 8.5)	14.9 (13.9, 15.9)	22.9 (21.6, 24.4)
Lymph node					
Negative	3755	313	3.3 (2.8, 3.9)	7.0 (6.1, 7.9)	11.7 (10.4, 13.1)
Positive	5453	693	5.8 (5.2, 6.5)	10.9 (10.0, 11.8)	16.7 (15.5, 18.1)
Surgery					
Breast-conserving surgery	4310	418	4.3 (3.8, 5.0)	7.9 (7.1, 8.9)	13.0 (11.8, 14.4)
Mastectomy	5738	853	6.8 (6.1, 7.5)	13.1 (12.2, 14.1)	19.8 (18.5, 21.2)
Neoadjuvant					
Chemo	557	64	7.9 (5.9, 10.6)	12.0 (9.3, 15.3)	16.4 (12.5, 21.4)
Trastuzumab	112	≤10	6.7 (3.3, 13.6)	9.1 (4.8, 16.9)	9.1 (4.8, 16.9)
Adjuvant					
Chemo	3236	243	3.3 (2.7, 3.9)	6.3 (5.4, 7.3)	9.9 (8.7, 11.3)
Trastuzumab	697	45	2.8 (1.8, 4.3)	6.4 (4.7, 8.8)	8.0 (5.9, 10.7)
ER+ and/or PR+					
Trastuzumab	400	19	2.3 (1.2, 4.3)	4.7 (2.9, 7.6)	5.7 (3.6, 9.1)
No trastuzumab	7443	789	4.3 (3.9, 4.8)	8.8 (8.1, 9.5)	14.6 (13.5, 15.7)
ER- and PR-					
Trastuzumab	296	26	3.8 (2.1, 6.8)	9.2 (6.2, 13.7)	10.7 (7.3, 15.8)
No trastuzumab	1463	342	13.2 (11.5, 15.1)	21.1 (18.9, 23.5)	30.3 (27.4, 33.4)

CONCLUSIONS

- Linking SEER and Medicare allowed us to assess mortality according to tumor characteristics and cancer treatments, respectively, which are both related to prognosis.
- Unadjusted analyses demonstrate that the risk of death is highest among a group of women who are ER-/PR- and do not receive trastuzumab treatment, which we infer to indicate the "triple negative" phenotype, confirming findings from other studies and emphasizing the need for novel approaches to this patient population.
- Older patients (75 or older) also faired worse, and may be exacerbated by comorbidities found in this elderly population.
- The use of neoadjuvant therapy in the population was fairly low at 5%. Survival was lower among the neoadjuvant treated patients than the adjuvant treated patients, likely due to differing severity of underlying disease.
- The use of administrative data from Medicare should be further enhanced with inclusion of test results from standard gene expression panels, which provide additional level of granularity including luminal A and luminal B phenotypes. Availability of these data would help to ensure a better match of therapy for the patient and adequate assessment of resource utilization.

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