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# Higher-risk breast cancer in women aged 80 and older: Exploring the effect of treatment on survival

Abdulla Al-Rashdan [a, b], Yuan Xu [a, b, c, d], May Lynn Quan [a, b, c, d], Jeffrey Q. Cao [a, b], Winson Cheung [a, b, c], Antoine Bouchard-Fortier [a, b, d], Shiying Kong [e], Lisa Barbera [a, b, *]

[a] Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[b] Tom Baker Cancer Centre, Calgary, Alberta, Canada
[c] Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[d] Department of Surgery, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[e] The Department of Analytics, Alberta Health Services, Calgary, Alberta, Canada

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ABSTRACT

*Background:* To understand the association between various treatments and survival for older women with higher-risk breast cancer when controlling for patient and tumor factors.
*Materials and methods:* We conducted a retrospective, population-based study. Women aged 80 years or older and diagnosed between 2004 and 2017 with non-metastatic, higher-risk breast cancer were identified form the provincial cancer registry in Alberta, Canada. Higher-risk was defined as any of following: T3/4, node positive, human epidermal factor receptor-2 (Her2) positive or triple negative disease. Treatments were surgery, radiotherapy and systemic therapy (hormonal therapy, and/or chemotherapy and/or trastuzumab) or a combination of the previous. Cox regression models were used to examine the association between treatments and breast cancer specific survival (BCSS) and overall survival (OS).
*Results:* 1369 patients were included. The median age was 84 years. 332 (24%) of women had T3-T4 tumors, 792 (58%) had nodal involvement, 130 (10%) had Her2 positive tumors, 124 (9%) had triple negative tumors. After a median follow-up of 35 months, 29.5% of patients died of breast cancer whereas 34.2% died from other causes. Patients had a lower adjusted hazard for BCSS if they had surgery (hazard ratio [HR] = 0.37 95% confidence interval [CI]: 0.27, 0.51), or systemic therapy (HR = 0.75, 95%CI: 0.58, 0.98). Patients had an increased probability of breast cancer death in the first 5 years after diagnosis compared to death from other causes.
*Conclusions:* Surgery and systemic therapy were associated with longer BCSS and OS. This suggests that maximizing treatments might benefit higher-risk patients.


## 1. Introduction

An increasing number of women aged 80 years or older are being diagnosed with breast cancer as a consequence of the growing, aging population in North America [1]. This is expected to rise even more in the coming years [2]. However, unlike younger patients, management of the oldest old is complex [3]. It can be challenging to weigh the competing risks of death from cancer versus death from another cause. Patient preferences also change with age with an emphasis on quality of life [4,5]. Comorbidities and frailty may affect treatment tolerability [6]. Some patients may not have the same social and emotional support as their younger counterparts [7], and physicians' treatment recommendations may be influenced by older age, leading to under-treatment [8].

Treatment recommendations for patients aged 80 years or older have been minimally driven by prospective evidence as these patients are rarely represented in clinical trials [9,10], and management is extrapolated from prospective evidence in younger populations. Retrospective evidence is limited by low patient numbers [11–22] or a lack of information on how various

*Abbreviations:* Her2, human epidermal factor receptor-2; BCSS, breast cancer specific survival; OS, overall survival; HR, hazard ratio; CI, confidence interval.

* Corresponding author. Division of Oncology, Tom Baker Cancer Centre, 1331 29 St NW, Calgary, AB, T2N 4N2, Canada.
*E-mail address:* lisa.barbera@albertahealthservices.ca (L. Barbera).

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contemporary treatment strategies affect the disease trajectory [23–26]. Moreover, most studies focus on patients with lower-risk, small, hormone positive tumors [11–26]. Women with higher-risk, locally advanced or biologically unfavorable disease, are represented much less frequently.

Women with higher-risk disease experience a more aggressive course with a higher probability of progression and a lower probability of disease specific survival in contrast to the lower-risk patients [27]. In older patients with higher-risk disease, the association between treatment choices and cancer survival is not well described. Understanding this association would help tailor management, aiming to minimize over- or under-treatment [28]. The purpose of this study was to characterize treatment patterns and their associated cancer specific and overall survival in older women with higher-risk breast cancer.

## 2. Methods

### 2.1. Study design, settings and cohort creation

This is a retrospective, population-based cohort study using observational data of breast cancer patients treated in Alberta, Canada. Eligibility criteria included women aged 80 years or older and diagnosed with higher-risk breast cancer between January 1st, 2004 and December 31st, 2017. Patients were excluded if they were male, had ductal carcinoma in situ only or had distant metastases. Higher-risk disease was defined as having any of the following: locally advanced T category (T3 or 4), any node positive tumor (N+), human epidermal factor receptor-2 (Her2) positive or triple negative disease. We followed the STROBE guidelines for reporting this study [29]. Ethics approval was obtained from the Health Research Ethics Board of Alberta—Cancer Committee (HREBA.CC-18-0166).

### 2.2. Data sources and covariates

The province of Alberta has a single-payer, universal health care system. Cancer diagnoses are captured and can be retrospectively linked to administrative healthcare data. We used the following databases: the Alberta Cancer Registry (ACR), which captures demographics, disease characteristics, treatment details and vital statistics. The ACR is certified by the North American Association of Central Cancer Registries and has received a gold certification based on completeness of the data among other measures that judge data quality [30]. Other databases included the Discharge Abstract Database (DAD), which captures information about hospitalizations at acute care institutions, the National Ambulatory Care Reporting System (NACRS), which captures information from outpatient and emergency room visits, and the Provincial Physician Billing Claims dataset that was used to define the type of surgery. Finally, the 2011 census [31] with postal code linkage [32] was used to estimate neighborhood levels of education and income as well as rurality.

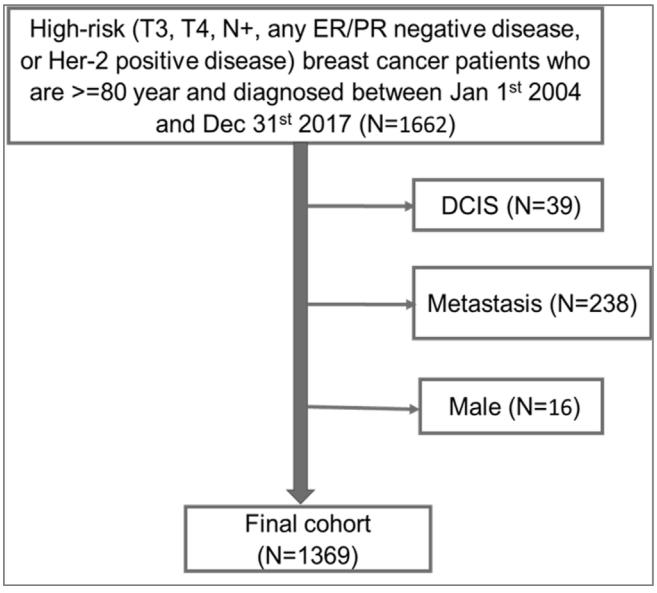


**Fig. 1.** Consort diagram.

Covariates included age at diagnosis. Length of follow-up was defined as the difference, in months, between the date of last follow-up and the date of diagnosis. Charlson Comorbidity Index (CCI) was generated through a validated claims-based algorithm [33]. Income quintiles were defined as median community income that was linked to the patient's residence with 1 representing the lowest and 5 the highest income quintile. Education quintiles were defined based on the percentage of residents who had a high school degree or higher based on census data, with 1 representing the lowest percentage of high school education compared to 5 which represents the highest. Rurality was defined as a binary variable based on postal code data per the Alberta Health Services local geography boundaries.

The T, N and M stages were retrieved from the ACR. The ACR uses algorithms to generate a collaborative stage relying on pathological data first, then clinical data, including imaging and clinical notes, to formulate a best stage [30]. Prior to 2010, stage was reported according to the American Joint Committee on Cancer (AJCC), sixth edition, and after 2010, it was reported according to the AJCC, seventh edition. The grade was also retrieved from the ACR as Modified Bloom-Richardson grade. The estrogen receptor (ER), progesterone receptor (PR) and Her2 status were retrieved from the ACR as binary variables (positive/negative). Before 2010, Her2 was not routinely tested in Alberta, therefore, the majority of those with missing Her2 status are patients diagnosed before 2010.

Treatment covariates included surgery, radiotherapy, systemic therapy (chemotherapy and/or trastuzumab, and/or hormonal therapy) reported as a binary variable (yes/no) and are captured in ACR. All treatment covariates captured are for primary treatment only and do not include treatment for recurrence. We classified combined treatment options into four categories: a no treatment category defined as no treatment or non-definitive local (radiotherapy) treatment, systemic treatment only without definitive local treatment defined as hormonal therapy, and/or chemotherapy and/or trastuzumab without surgery. Definitive local treatment only defined as surgery with or without radiotherapy and no adjuvant systemic therapy, and definitive local and adjuvant systemic treatment category defined as surgery with or without radiotherapy and adjuvant systemic therapy.

### 2.3. Outcome definition

Our primary outcome was breast cancer specific survival (BCSS), which is defined the time from diagnosis to death from breast cancer over the study period until the last day of follow-up. Death caused by cancer is captured from the ACR through the International Classification of Disease, Ninth edition (174 code) and Tenth edition, (C50 code) [34]. Death codes are based on information retrieved from the death certificate. Secondary outcomes were overall survival (OS) and the cumulative probability of death by cause (breast cancer vs other). The last follow-up date was July 30th, 2019 and after that patients who were alive were censored.

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

| | Alive (N = 496) | P-value | Non-Breast Cancer Death (N = 468) | P-value | Breast Cancer Death (N = 405) | P-value | Total (N = 1369) |
|---|---|---|---|---|---|---|---|
| **Age at diagnosis** | | | | | | | |
| Median (IQR[a]) | 83 (81−86) | <.0001 | 85 (83−89) | <.0001 | 84 (82−88) | 0.3988 | 84 (82−88) |
| **Age group** | | | | | | | |
| 80-85 | 341 (68.8%) | <.0001 | 240 (51.3%) | <.0001 | 236 (58.3%) | 0.4452 | 817 (59.7%) |
| 86-90 | 128 (25.8%) | | 146 (31.2%) | | 114 (28.1%) | | 388 (28.3%) |
| 91-95 | 25 (5%) | | 70 (15%) | | 51 (12.6%) | | 146 (10.7%) |
| >95 | 2 (0.4%) | | 12 (2.6%) | | 4 (1%) | | 18 (1.3%) |
| **Length of follow-up (m [b])** | | | | | | | |
| Median (IQR[b]) | 37.5 (16.9−72.4) | 0.2379 | 43.1 (20.4−81) | <.0001 | 25 (12.6−49.1) | <.0001 | 34.8 (16−67.7) |
| **CCI Score** | | | | | | | |
| 0 | 197 (39.7%) | <.0001 | 116 (24.8%) | <.0001 | 140 (34.6%) | 0.7331 | 453 (33.1%) |
| 1 | 132 (26.6%) | | 123 (26.3%) | | 106 (26.2%) | | 361 (26.4%) |
| >=2 | 167 (33.7%) | | 229 (48.9%) | | 159 (39.3%) | | 555 (40.5%) |
| **Rurality** | | | | | | | |
| Rural | 99 (20%) | 0.0069 | 113 (24.1%) | 0.98 | 118 (29.1%) | 0.0048 | 330 (24.1%) |
| Urban | 397 (80%) | | 355 (75.9%) | | 287 (70.9%) | | 1039 (75.9%) |
| **Education Q [c]** | | | | | | | |
| 1 | 58 (11.7%) | <.0001 | 83 (17.7%) | 0.0417 | 82 (20.2%) | 0.0835 | 223 (16.3%) |
| 2 | 88 (17.7%) | | 101 (21.6%) | | 77 (19%) | | 266 (19.4%) |
| 3 | 88 (17.7%) | | 94 (20.1%) | | 80 (19.8%) | | 262 (19.1%) |
| 4 | 156 (31.5%) | | 96 (20.5%) | | 97 (24%) | | 349 (25.5%) |
| 5 | 106 (21.4%) | | 94 (20.1%) | | 69 (17%) | | 269 (19.6%) |
| **Income Q [c]** | | | | | | | |
| 1 | 61 (12.3%) | 0.0087 | 83 (17.7%) | 0.1171 | 67 (16.5%) | 0.6397 | 211 (15.4%) |
| 2 | 86 (17.3%) | | 107 (22.9%) | | 87 (21.5%) | | 280 (20.5%) |
| 3 | 112 (22.6%) | | 91 (19.4%) | | 86 (21.2%) | | 289 (21.1%) |
| 4 | 118 (23.8%) | | 95 (20.3%) | | 75 (18.5%) | | 288 (21%) |
| 5 | 119 (24%) | | 92 (19.7%) | | 90 (22.2%) | | 301 (22%) |
| **Provincial Zone Name** | | | | | | | |
| Calgary | 180 (36.3%) | 0.1482 | 147 (31.4%) | 0.1112 | 134 (33.1%) | 0.0302 | 461 (33.7%) |
| Central | 61 (12.3%) | | 70 (15%) | | 72 (17.8%) | | 203 (14.8%) |
| Edmonton | 170 (34.3%) | | 155 (33.1%) | | 122 (30.1%) | | 447 (32.7%) |
| North | 33 (6.7%) | | 29 (6.2%) | | 39 (9.6%) | | 101 (7.4%) |
| South | 52 (10.5%) | | 67 (14.3%) | | 38 (9.4%) | | 157 (11.5%) |
| | **Alive (N=496)** | P-value | **Non-Breast Cancer Death (N=468)** | P-value | **Breast Cancer Death (N=405)** | P-value | **Total (N=1369)** |
| **Grade** | | | | | | | |
| 1 | 64 (12.9%) | 0.0001 | 59 (12.6%) | 0.0071 | 22 (5.4%) | <.0001 | 145 (10.6%) |
| 2 | 227 (45.8%) | | 223 (47.6%) | | 143 (35.3%) | | 593 (43.3%) |
| 3 | 194 (39.1%) | | 163 (34.8%) | | 199 (49.1%) | | 556 (40.6%) |
| Unknown | 11 (2.2%) | | 23 (4.9%) | | 41 (10.1%) | | 75 (5.5%) |
| **T Stage** | | | | | | | |
| T1 | 188 (37.9%) | <.0001 | 137 (29.3%) | 0.8265 | 91 (22.5%) | <.0001 | 416 (30.4%) |
| T2 | 222 (44.8%) | | 209 (44.7%) | | 170 (42%) | | 601 (43.9%) |
| T3 | 53 (10.7%) | | 61 (13%) | | 49 (12.1%) | | 163 (11.9%) |
| T4 | 32 (6.5%) | | 55 (11.8%) | | 82 (20.2%) | | 169 (12.3%) |
| Unknown | 1 (0.2%) | | 6 (1.3%) | | 13 (3.2%) | | 20 (1.5%) |
| **N Stage** | | | | | | | |
| N0 | 231 (46.6%) | <.0001 | 182 (38.9%) | 0.9976 | 113 (27.9%) | <.0001 | 526 (38.4%) |
| N1 | 202 (40.7%) | | 186 (39.7%) | | 160 (39.5%) | | 548 (40%) |
| N2 | 46 (9.3%) | | 55 (11.8%) | | 58 (14.3%) | | 159 (11.6%) |
| N3 | 13 (2.6%) | | 28 (6%) | | 44 (10.9%) | | 85 (6.2%) |
| Unknown | 4 (0.8%) | | 17 (3.6%) | | 30 (7.4%) | | 51 (3.7%) |
| **Receptor Status** | | | | | | | |
| ER[d] + ve[g] or PR[e] + ve[g] & Her2[f] -ve[h]/unknown | 357 (72%) | <.0001 | 335 (71.6%) | 0.0129 | 254 (62.7%) | <.0001 | 946(69.1%) |

(*continued on next page*)

**Table 1** (*continued*)

| | Alive (N=496) | P-value | Non-Breast Cancer Death (N=468) | P-value | Breast Cancer Death (N=405) | P-value | Total (N=1369) |
|---|---|---|---|---|---|---|---|
| Her2[f] Positive | 65 (13.1%) | | 31 (6.6%) | | 34 (8.4%) | | 130 (9.5%) |
| Triple Negative | 52 (10.5%) | | 34 (7.3%) | | 38 (9.4%) | | 124 (9.1%) |
| ER[d] −ve[h] & PR −ve[h] & Her2[f] unknown | 18 (3.6%) | | 52 (11.1%) | | 54 (13.3%) | | 124 (9.1%) |
| Unknown[i] | 4 (0.8%) | | 16 (3.4%) | | 25 (6.2%) | | 45 (3.2%) |
| **Surgery** | | | | | | | |
| No | 36 (7.3%) | <.0001 | 76 (16.2%) | 0.6953 | 103 (25.4%) | <.0001 | 215 (15.7%) |
| Yes | 460 (92.7%) | | 392 (83.8%) | | 302 (74.6%) | | 1154 (84.3%) |
| **Radiotherapy** | | | | | | | |
| No | 326 (65.7%) | <.0001 | 371 (79.3%) | <.0001 | 294 (72.6%) | 0.9129 | 991 (72.4%) |
| Yes | 170 (34.3%) | | 97 (20.7%) | | 111 (27.4%) | | 378 (27.6%) |
| **Systemic Therapy** | | | | | | | |
| No | 228 (46%) | <.0001 | 274 (58.5%) | 0.02 | 240 (59.3%) | 0.0149 | 742 (54.2%) |
| Yes | 268 (54%) | | 194 (41.5%) | | 165 (40.7%) | | 627 (45.8%) |

Abbreviations, [a] Interquartile Range, [b] Months, [c] Quintiles, [d] Estrogen Receptor, [e] Progesterone Receptor; [f] Human Epidermal Growth Factor Receptor 2, [g] Positive, [h] Negative, [i] two or more unknown receptor status.

### 2.4. Statistical analyses

We conducted descriptive analysis for our cohort. Survival was estimated through the Kaplan Meier (K-M) method. To minimize bias, we conducted sensitivity analysis for BCSS, OS on four models. The first two models were generated to see if the missing Her2 status affected the outcomes while models 3 and 4 were to eliminate patients who did not have surgery for any reason including those with poor prognostic factors that affected their survival such as comorbidities, and to assess whether extent of treatment affected survival in those who were to tolerate treatment. Model 1 included the whole cohort and defined hormonal receptor status as positive or negative, while ignoring Her2 status. Model 2 evaluated the sub-group with known Her2 status and defined hormonal receptor status as positive or negative and included a Her2 status variable (positive/negative). Model 3 included the subgroup of patients who had surgery and defined biologic status as in Model 1. Model 4 included patients treated with surgery and whose Her2 status was known and defined biologic status as in Model 2. Associations between patient, tumor and treatment variables, and survival were assessed through univariable analysis including T test for continuous variable and Chi-square for categorical variables. Multivariable Cox regression analysis was used to assess the independent factors associated with breast cancer specific survival and overall survival, adjusting for possible confounders including age in 5-year increments, CCI score, education quintile, income quintile, rurality, treatment zone, T-category, N-category, receptor group, grade, and treatment type. Also, we calculated the cumulative risk of death due to breast cancer vs other causes. All the data manipulation, linkages, and analyses were done in SAS 9.4 (SAS Institute, Cary, NC).

## 3. Results

### 3.1. Patient, tumor and treatment characteristics

1369 patients met the inclusion criteria (Fig. 1). The median age for the entire cohort was 84 years (interquartile range [IQR], 82–88). The majority of our population (1205 [88%]) were between 80 and 90 years of age whereas 164 (12%) were older than 91. 555 (40.5%) patients had CCI scores of 2 or more. The distribution of patients' characteristics can be seen in Table 1.

The majority of patients had stage II-III disease (663 [48%], 422 [31%]) of which 332 (24%) had T3-T4 tumors, 792 (58%) had nodal involvement, 130 (10%) had Her2 positive tumors, and 124 (9%) had triple negative tumors.

For the whole cohort, 1154 patients (84%) had surgery, 378 patients (27.6%) received radiotherapy, and 627 patients (45.8%) received systemic therapy of which 32 patients received chemotherapy and 12 received trastuzumab. The patient distribution in the treatment categories were: 88 (6.4%) patients had no treatment, 115 (8.4%) had systemic treatment alone, 545 (39.8%) had definitive local treatment only, and 621 (45.3%) had definitive local and adjuvant systemic treatment.

### 3.2. Survival with individual treatments

After a median follow-up of 35 months, 873 (63.7%) patients had died; 405 (46%) of deaths were due to breast cancer affecting 29.5% of the total cohort whereas the reminder of deaths (54%) were from other causes affecting 34.2% of the total cohort. Individual treatment factors associated with improved BCSS on multivariable analysis for the whole cohort in model 1 were; surgery (hazard ratio [HR] = 0.37, 95% confidence interval [CI]: 0.27, 0.51) ($p < 0.0001$), and systemic therapy (HR = 0.75, 95%CI: 0.58, 0.98,

**Table 2**
Multivariable analysis of Breast Cancer Specific Survival and Overall survival in Model 1.

| Category | Breast Cancer Specific Survival Hazard Ratio (95% CI[a]) | Overall Survival Hazard Ratio (95% CI[a]) |
|---|---|---|
| Age group | | |
| 80–85 | Reference | Reference |
| 86–90 | 1.03 (0.81–1.31) | **1.3 (1.1 to 1.52)** |
| 91–95 | 1.38 (0.99–1.92) | **2.06 (1.66 to 2.57)** |
| >95 | 1.26 (0.46–3.48) | **3.47 (2.06 to 5.83)** |
| **CCI Score** | | |
| 0 | Reference | Reference |
| 1 | 1.14 (0.88–1.47) | **1.36 (1.14 to 1.64)** |
| >=2 | 1.22 (0.96–1.56) | **1.85 (1.56 to 2.19)** |
| **Grade** | | |
| 1 | Reference | Reference |
| 2 | **1.99 (1.26 to 3.14)** | **1.42 (1.11 to 1.82)** |
| 3 | **3.58 (2.26 to 5.7)** | **2 (1.54 to 2.59)** |
| Unknown | **3.66 (2.09 to 6.41)** | **1.96 (1.36 to 2.82)** |
| **T Stage** | | |
| T1 | Reference | Reference |
| T2 | **1.34 (1.03 to 1.76)** | **1.3 (1.09 to 1.55)** |
| T3 | **1.49 (1.03 to 2.16)** | **1.45 (1.14 to 1.85)** |
| T4 | **1.97 (1.39 to 2.79)** | **1.61 (1.25 to 2.06)** |
| Unknown | 1.51 (0.78–2.95) | 1.43 (0.86–2.39) |
| **N Stage** | | |
| N0 | Reference | Reference |
| N1 | **1.37 (1.06 to 1.76)** | 1.13 (0.96–1.34) |
| N2 | **1.66 (1.17 to 2.37)** | **1.31 (1.03 to 1.68)** |
| N3 | **3.36 (2.29 to 4.94)** | **2.81 (2.12 to 3.72)** |
| Unknown | **2.37 (1.51 to 3.71)** | **1.54 (1.11 to 2.15)** |
| **Surgery** | | |
| No | Reference | Reference |
| Yes | **0.37 (0.27 to 0.51)** | **0.5 (0.4 to 0.62)** |
| **Radiotherapy** | | |
| No | Reference | Reference |
| Yes | 0.93 (0.73–1.2) | **0.83 (0.69 to 0.98)** |
| **Systemic Therapy** | | |
| No | Reference | Reference |
| Yes | **0.75 (0.58 to 0.98)** | **0.67 (0.56 to 0.81)** |

Abbreviations [a] Confidence Interval, [b] Charlson Comorbidity Index,Bolded results represent a statistically significant difference.

p = 0.0354) (Table 2), and those factors remained significant in model 2 (Supplementary Table 1, Appendix).Treatment factors associated with longer OS on multivariable analysis for model 1 were surgery (HR = 0.5, 95%CI: 0.4 to 0.62, p < 0.0001), which remained significant in model 2, radiotherapy (HR = 0.83, CI: 0.69 to 0.98, p = 0.0322), which remained significant in Model 3, and systemic therapy (HR = 0.75 (CI: 0.58 to 0.98, p < 0.0001), which remained significant in model 3. Patient and tumor factors associated with BCSS and OS were as expected for model 1. Interestingly, receptor status was not associated with BCSS or OS in all models.

### 3.3. Survival with combined treatment categories

For the combined treatment categories, patients had a significantly improved BCSS (p < 0.0001) and OS (p < 0.0001) in the whole cohort if they had definitive local treatment only or definitive local and adjuvant systemic treatment in comparison to systemic treatment only or no treatment categories. (Fig. 2). Similar observations were seen in the cohort of known Her2 patients. The sub-groups of patients treated with definitive local treatment only confirmed that BCSS (p = 0024) and OS (p < 0.0001) were significantly improved with the addition of adjuvant systemic treatment to definitive local treatment.

### 3.4. Cumulative probability of death

When comparing the cumulative probability of death from breast cancer versus death from other causes for the whole cohort, we observed a higher cumulative probability of dying from breast cancer than dying from other causes in the first 5 years of follow-up. Also, higher proportion of patients who were treated with systemic treatment only or nothing died of breast cancer compared to the proportion of patients treated with definitive local with/without adjuvant systemic treatment (Fig. 3).

## 4. Discussion

Older women with higher-risk breast cancer who were treated with surgery or systemic treatment had improved BCCS and OS when controlling for patient and tumor factors. The cumulative probability of death from breast cancer was higher than the probability of death from other causes in the first 5 years after diagnosis in this higher-risk population. This suggests that more aggressive treatment might benefit such patients who can tolerate it.

Our study addresses a gap in the literature about the management of older patients with aggressive disease features in a contemporary era. Current evidence is lacking due to the absence of clinical trials that include such patients and the limitation of the published retrospective evidence which includes only a small number of such patients.

The results of this study demonstrate a worse outcome for this cohort than other studies in the literature. Reasons for the difference might be due to patient selection as many studies reported on a small population and lacked or minimally included patients with locally advanced or biologically unfavorable disease (Supplementary Table 2, Appendix). Comparisons are also marred by differences in the staging systems used and what treatments were used and how they were defined [23,24]. Additionally, some studies were limited by missing disease and treatment information that might affect outcome [23–25].

Surgery was associated with fewer breast cancer deaths in our population. Surgical treatment rates in older women are varied in the literature, ranging from 54% to 100% [11–26], with surgery typically associated with a lower cancer death rate. One study of stage II patients demonstrated that patients who were not treated with surgery had a higher hazard of breast cancer death than death from other causes when compared to patients treated with surgery and radiotherapy [24]. This suggests additional treatment strategies should be considered in higher-risk patients who cannot have surgery. Unlike younger populations with higher-risk disease, radiotherapy was underutilized in our study similar to what is previously reported [22].

We grouped systemic therapies in one category since the majority of patients in this category received hormonal therapy. Our results suggest that systemic treatment was better than no treatment. However, it was associated with inferior survival when surgery was not performed. While a meta-analysis [35] showed that there was no significant survival difference between primary hormonal treatments vs. surgery, it included trials of patients with early stage and favorable biology. In our study, systemic therapy was associated with better BCSS and OS, in the adjuvant setting. Although the majority of Her2 positive and triple negative patients did not receive chemotherapy or trastuzumab, they did not have worse survival compared to the ER/PR positive patients in our study.

The limitations of our study include its retrospective design and the risk of selection bias. Interestingly, our study showed that breast cancer death was higher in patients receiving non-surgical options which suggests that even for patients who were not selected to receive surgery, breast cancer played a larger role contributing to their death. Another limitation is our inability to adjust for patient preference and factors that affect survival in

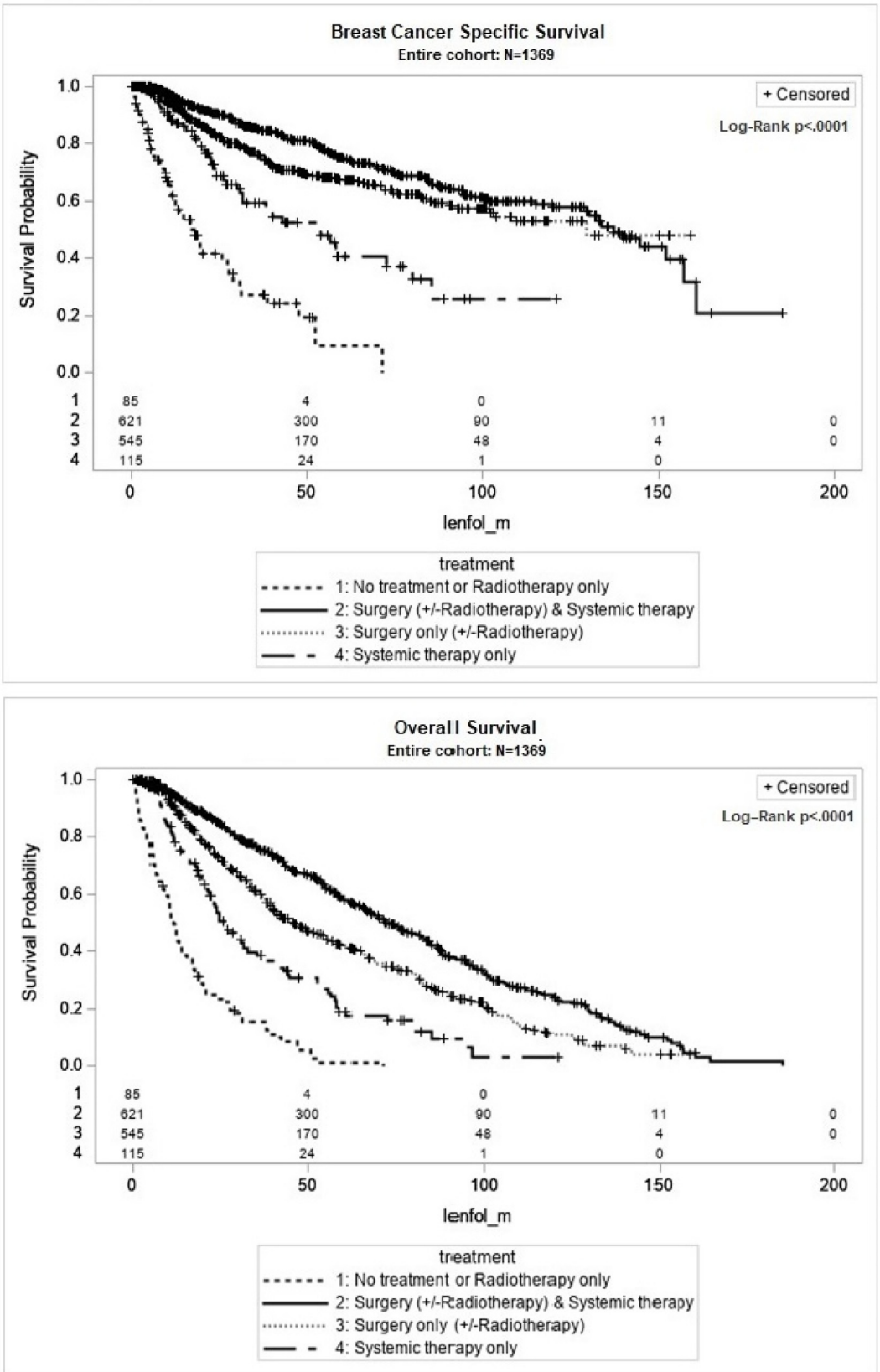


**Fig. 2.** Kaplan-Meier curves of breast cancer specific survival (BCSS) and overall survival (OS) for the entire cohort.

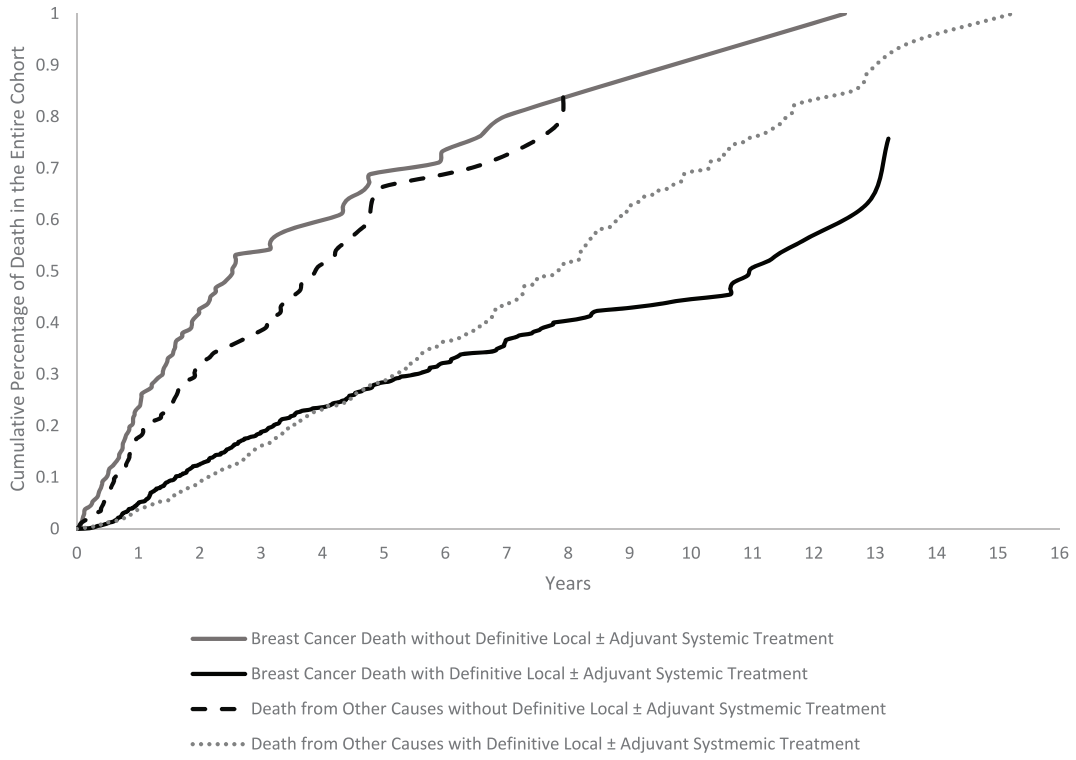


**Fig. 3.** Cumulative probability of death (breast cancer vs. other causes) by treatment category.

geriatric population such as performance status, frailty, geriatric syndromes and social barriers, which cannot be retrieved from administrative databases. Finally, we could not report on the adjuvant treatment compliance, which might lead to altered treatment efficacy.

## 5. Conclusions

In a population of women aged 80 or older with higher-risk breast cancer, surgery and systemic therapy were associated with longer breast cancer specific and overall survival. This emphasizes the need for maximizing treatments delivered for carefully evaluated older patients eligible for more aggressive management.

## Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by YX, SK. The first draft of the manuscript was written by AR, LB, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## Ethics approval

Ethics approval was obtained from the Health Research Ethics Board of Alberta—Cancer Committee (HREBA.CC-18-0166). The study was performed in accordance with the.

## Declaration of Helsinki

The manuscript is in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. The privacy rights of human subjects must always be observed. Informed consent is not applicable for this study.

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## Data statement

The research data is confidential.

## Declarations of competing interest

LB has received an honorarium from Genentech and travel support from Elekta. Other authors, none.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2021.07.005.

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