

## Original article

## Surgery for early breast cancer in the extremely elderly leads to improved outcomes – An Asian population study



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## ARTICLE INFO

## Article history:

Received 17 April 2017

Received in revised form

11 August 2017

Accepted 11 September 2017

Available online 22 September 2017

## Keywords:

Extremely elderly

Treatment

Surgery

Outcome

Survival

≥ 80 years

## ABSTRACT

**Aim:** The optimal treatment of breast cancer for extremely elderly patients (aged  $\geq 80$  years) is debatable. With an aging population, management of this group of patients will be increasingly common. This study aims to compare the survival outcomes of extremely elderly patients against younger ones, following different treatment modalities within each stage. The differences in treatment patterns across different stages have also been examined.

**Methods:** Female Singapore Citizens and Permanent Residents diagnosed with breast cancer from 2003 to 2014 were identified from the Singapore Cancer Registry. Patients were divided into 2 age groups, below 80, and 80 and above years old, and categorized into 3 main treatment groups, namely surgery, non-surgical treatment, and no treatment. Analysis was made on their survival outcomes.

**Results:** 19,314 patients were diagnosed with breast cancer during the 12-year study period. 1482 patients were excluded due to unknown stage. 673 patients were aged 80 years and above, while 17,159 patients were aged below 80. Elderly patients presented with later stages of disease, and were less likely to have surgery. In Stage I and II, the difference in 5-year breast cancer specific outcome following surgery, was small between the 2 age groups. Among the elderly group, surgery resulted in improved survival. Those who did not have surgery performed better with endocrine therapy than with no treatment.

**Conclusions:** Extremely elderly patients, especially those with Stages I and II breast cancer do not fare worse than younger patients, and should be offered surgery if they are fit.

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## 1. Introduction

Cancer accounted for 30% of deaths in Singapore in 2015, with breast cancer being the leading form of cancer among females [1]. Singaporean women have one of the highest life expectancy in the world. With a life expectancy of 84.9 years at birth, they could expect to live to 87.2 years [2] once they reach 65 years of age. It is estimated that by year 2050, 13.8% of Singapore's population will be aged more than 80 years [3]. In the 5-year period from 2010 to

2014, the incidence rate of breast cancer among those in this age group was 176.5 per 100,000 women-years [4], compared to 169.9 per 100,000 women-years in the period 2005–2009. This incidence rate will continue to rise as our population continues to age, significantly increasing the healthcare burden.

There are existing guidelines [5] that help to guide the management of breast cancer in elderly patients, but physicians still face challenges in identifying candidates for the appropriate management. Although surgery is potentially curative, extremely elderly patients are treated conservatively because of advanced age [6,7], presence of comorbidities, frailty, poor functional status or social support [6,8]. In our earlier study on the perioperative outcomes of therapeutic breast surgery on 109 patients above 80 years of age, we showed that general anaesthesia is well tolerated by this

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group of patients [9]. With only a 3% incidence of major complications, and no 30-day mortality, we concluded that surgery was safe, despite 90% of our patients having at least one comorbidity.

This study examines how treatment pattern differs between that in the extremely elderly patients and in those younger, and its impact on patient survival and disease control.

## 2. Methods

Female Singapore Citizens and Permanent Residents who were diagnosed with breast cancer from 2003 to 2014 were identified from the Singapore Cancer Registry (SCR), a division within the National Registry of Diseases Office (NRDO). The Singapore Cancer Registry is a population-based registry that was started in 1968. Comprehensive cancer registration was achieved through data obtained from a combination of sources: (a) notifications by the medical profession, (b) pathology records, (c) hospital records, and (d) mortality data from the Registry of Births and Deaths (RBD), Ministry of Home Affairs (MHA). Notification of cases of cancer has been mandatory since 2009. Staff of the Registry reviewed hospital discharges and death certificates for all cancer patients. The completeness of reporting is high: 96% in the 1970s and close to 100% in the 1990s. The proportion of death-certificate-only notifications was 4.2% for the period 1968 to 1977, 1.0% for 1993 to 1997 and 0.9% for 1998 to 2002 [10]. SCR records treatment within 6 months of diagnosis.

We examined the demographics and disease characteristics of patients in our study population at the point of diagnosis and treatment received within the first 6 months from diagnosis. Treatment was categorized into 3 groups: surgery, non-surgical treatment, and no treatment. Non-surgical treatment was defined as having at least one of the following therapies without surgery: endocrine, chemotherapy, radiation therapy or anti-HER2 therapy. All patients were similarly staged, using histopathological staging

for those who underwent surgery and clinical tumor staging for those who did not have surgery. From 2003 to 2009, the 6th edition American Joint Committee on Cancer (AJCC) classification system was used, while those diagnosed after 2010 were staged with the 7th edition AJCC classification system. Survival was estimated by the Kaplan-Meier method and log-rank tests were used to compare the overall survival (OS) and breast cancer specific survival (BCSS) in the extremely elderly ( $\geq 80$  years old) with those younger ( $< 80$  years old), stratified by cancer stage and treatment modality. Multivariate Cox regressions were performed to estimate the risk of dying from any cause and from breast cancer. Variables which were statistically significant in univariate analysis and those which were clinically relevant in predicting survival were included in the model. Those with unknown stage were excluded. Survival outcome by treatment was assessed for those with stage I to III disease. Data was censored on 31 December 2015.

Ethical approval for this study was obtained from Singapore's Ministry of Health as well as the Institutional Review Board. Data was analysed using STATA SE version 13.

## 3. Results

Between January 2003 and December 2014, 19,314 patients were diagnosed with breast cancer in Singapore. Eight hundred and forty-four patients were aged 80 years and above at diagnosis, while 18,470 patients were less than 80 years old. Table 1 shows the characteristics of the study population. The stage of disease was unknown in 171 (20.3%) for those aged  $\geq 80$  years, and 1311 patients (7.1%) for those  $< 80$  years of age and these were excluded from analysis.

The elderly cohort presented with later stages of disease with 41% in stage III and IV compared to 28.3% in those less than 80 years old. Surgery was performed in only 61.4% of elderly patients compared to 92.5% in younger patients with curative disease (stage

**Table 1**  
Characteristics of Study Population, n = 17,832.

	$\geq 80$ years old				$< 80$ years old											
	Stage I		Stage II		Stage III		Stage IV		Stage I		Stage II		Stage III		Stage IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
	137	(100)	260	(100)	167	(100)	109	(100)	5767	(100)	6542	(100)	3273	(100)	1577	(100)
<b>Ethnicity</b>																
Chinese	117	(85.4)	230	(88.5)	143	(85.6)	92	(84.4)	4999	(86.7)	5257	(80.4)	2450	(74.9)	1138	(72.2)
Malay	9	(6.6)	11	(4.2)	11	(6.6)	10	(9.2)	368	(6.4)	676	(10.3)	550	(16.8)	299	(19.0)
Indian	10	(7.3)	16	(6.2)	9	(5.4)	7	(6.4)	269	(4.7)	463	(7.1)	214	(6.5)	113	(7.2)
Others	1	(0.7)	3	(1.2)	4	(2.4)	0	0.0	131	(2.3)	146	(2.2)	59	(1.8)	27	(1.7)
<b>Other cancer</b>																
Yes	23	(16.8)	32	(13.5)	20	(12.0)	8	(7.3)	412	(7.1)	390	(6.0)	184	(5.6)	71	(4.5)
No	114	(83.2)	225	(86.5)	147	(88.0)	101	(92.7)	5355	(92.9)	6152	(94.0)	3089	(94.4)	1506	(95.5)
<b>Laterality<sup>a</sup></b>																
Unilateral	108	(87.1)	194	(81.5)	129	(86.0)	79	(84.0)	4414	(88.1)	4975	(87.5)	2445	(87.2)	1144	(81.6)
Bilateral	2	(1.6)	4	(1.7)	6	(4.0)	3	(3.2)	41	(0.8)	69	(1.2)	57	(2.0)	67	(4.8)
Unknown	14	(11.3)	40	(16.8)	15	(10.0)	12	(12.8)	555	(11.1)	640	(11.3)	301	(10.7)	191	(13.6)
<b>Treatment</b>																
<b>Surgery + Adjuvant-</b>	102	(74.5)	152	(58.5)	92	(55.1)	20	(18.4)	5496	(95.3)	6128	(93.7)	2793	(85.3)	356	(22.6)
Radiotherapy	6	(5.9)	14	(9.2)	37	(40.2)	7	(35.0)	2044	(37.2)	1762	(28.8)	1321	(47.3)	115	(32.3)
Chemotherapy	1	(1.0)	2	(1.3)	7	(7.6)	4	(20.0)	1491	(27.1)	3927	(64.1)	2226	(79.7)	230	(64.6)
Hormonal therapy	47	(46.1)	84	(55.3)	60	(65.2)	10	(50.0)	2841	(51.7)	2475	(40.4)	853	(30.5)	174	(48.9)
Biological therapy	0	0.0	0	0.0	1	(1.1)	0	0.0	89	(1.6)	203	(3.3)	136	(4.9)	26	(7.3)
Nil adjuvant	50	(49.0)	59	(38.8)	21	(22.8)	7	(35.0)	1310	(23.8)	967	(15.8)	261	(9.3)	36	(10.1)
<b>Non-surgery treatment</b>	27	(19.7)	84	(32.3)	57	(34.1)	62	(56.9)	87	(1.5)	239	(3.6)	380	(11.6)	1047	(66.4)
Hormonal only	26	(96.3)	82	(97.6)	48	(84.2)	54	(87.1)	42	(48.3)	77	(32.2)	80	(21.1)	531	(50.7)
Non-hormonal	1	(3.7)	2	(2.4)	9	(15.8)	8	(12.9)	45	(51.7)	162	(67.8)	300	(78.9)	516	(49.3)
<b>No treatment</b>	8	(5.8)	24	(9.2)	18	(10.8)	27	(24.8)	184	(3.2)	175	(2.7)	100	(3.1)	174	(11.0)

% are computed with denominator = patients with surgery; patients can have a combination of treatment (ie. surgery + radiotherapy + chemotherapy), so the % may add up to  $> 100\%$ .

<sup>a</sup> Information available after 2005.

**Table 2**  
Five-year survival rate by stage and age group.

	5-Year Survival Rate* (%)			
	All Cause		Breast Cancer Specific	
	≥80	<80	≥80	<80
<b>Stage I</b>	(n = 117)	(n = 5613)	(n = 130)	(n = 5696)
Overall	85.4	97.3	94.9	98.8
Surgery	89.2 (91)	97.8 (5373)	96.1 (98)	99 (5440)
Non-surgery	74.1 (20)	81.6 (71)	92.6 (25)	92 (80)
No treatment	75 (6)	91.9 (169)	87.5 (7)	95.7 (176)
<b>Stage II</b>	(n = 176)	(n = 6045)	(n = 229)	(n = 6170)
Overall	67.7	92.4	88.1	94.3
Surgery	79 (120)	93.2 (5710)	92.1 (140)	94.9 (5814)
Non-surgery	54.8 (46)	80.8 (193)	85.7 (72)	86.2 (206)
No treatment	41.7 (10)	81.1 (142)	70.8 (17)	85.7 (150)
<b>Stage III</b>	(n = 81)	(n = 2564)	(n = 107)	(n = 2643)
Overall	48.5	78.3	64.1	80.8
Surgery	56.5 (52)	80.1 (2236)	65.2 (60)	82.4 (2300)
Non-surgery	38.6 (22)	70.5 (268)	64.9 (37)	73.2 (278)
No treatment	38.9 (7)	60 (60)	55.6 (10)	65 (65)

\*Survival was estimated by the Kaplan-Meier method and log-rank test; (Number of survivors at 5 years from diagnosis).

I–III). This difference was most marked in those with stage II disease, with a 35% mismatch between the 2 groups and close to half of the elderly patients with stage III disease did not have surgery (Table 1). Elderly patient were less likely to have adjuvant therapy

in addition to surgery: 10 (2.9%) had chemotherapy, 57 (16.5%) had radiotherapy while 191 (55.2%) had hormonal therapy, compared to younger patients: 7644 (53.0%) had chemotherapy, 5127 (35.6%) had radiotherapy while 6169 (42.8%) had hormonal therapy.

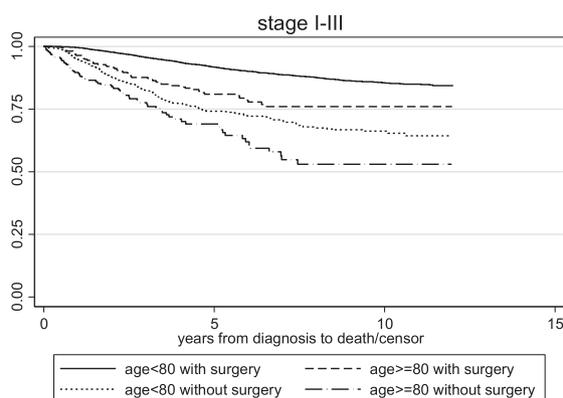
**Table 3**  
Risk of death by stage and population characteristics.

	Adjusted HR (95% CI)					
	All Cause			Breast Cancer Specific		
	Stage I	Stage II	Stage III	Stage I	Stage II	Stage III
<b>Age group</b>						
<80	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
≥80	4.93 (3.37–7.22)	4.20 (3.35–5.28)	2.65 (2.13–3.31)	3.18 (1.66–6.10)	1.68 (1.19–2.38)	1.63 (1.25–2.13)
<b>Other cancers</b>						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	7.16 (5.59–9.18)	2.45 (2.02–2.97)	1.27 (1.01–1.60)	1.71 (1.02–2.85)	0.88 (0.63–1.24)	0.81 (0.60–1.09)
<b>Ethnicity</b>						
Chinese	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Malay	1.90 (1.30–2.77)	1.55 (1.26–1.91)	1.28 (1.08–1.51)	1.92 (1.14–3.25)	1.58 (1.24–2.01)	1.20 (1.00–1.43)
Indian	1.18 (0.69–2.03)	1.32 (1.02–1.71)	1.17 (0.91–1.51)	0.80 (0.33–1.98)	1.47 (1.09–1.99)	1.26 (0.96–1.64)
Others	1.09 (0.48–2.45)	0.92 (0.55–1.54)	0.91 (0.53–1.58)	0.35 (0.05–2.47)	1.04 (0.59–1.85)	0.99 (0.56–1.75)
<b>Treatment (All patients)</b>						
Surgery	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Non-surgery	5.66 (3.72–8.62)	3.41 (2.69–4.34)	2.08 (1.74–2.49)	4.35 (2.31–8.17)	3.21 (2.36–4.36)	2.07 (1.71–2.52)
No treatment	2.57 (1.65–3.99)	3.16 (2.42–4.12)	2.47 (1.87–3.26)	3.37 (1.93–5.89)	3.24 (2.36–4.44)	2.32 (1.71–3.14)
<b>Treatment (≥80 group)</b>						
Surgery	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Non-surgery	1.80 (0.60–5.38)	3.18 (2.06–4.90)	1.27 (0.79–2.06)	1.40 (0.28–7.04)	3.28 (1.57–6.86)	0.89 (0.49–1.60)
No treatment	2.74 (0.61–12.38)	4.70 (2.66–8.28)	1.87 (0.97–3.61)	2.64 (0.31–22.21)	5.98 (2.58–13.87)	1.78 (0.84–3.78)
<b>Treatment (&lt;80 group)</b>						
Surgery	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Non-surgery	5.90 (3.66–9.52)	3.50 (2.61–4.68)	2.17 (1.79–2.63)	5.02 (2.54–9.95)	3.27 (2.32–4.61)	2.27 (1.85–2.79)
No treatment	2.62 (1.65–4.17)	2.49 (1.82–3.41)	2.61 (1.92–3.55)	3.46 (1.94–6.18)	2.78 (1.95–3.97)	2.39 (1.72–3.34)
<b>Stage (All patients)</b>						
I	1.00 (ref)			1.00 (ref)		
II	2.58 (2.25–2.95)			3.69 (3.06–4.46)		
III	6.37 (5.57–7.28)			11.49 (9.56–13.80)		
<b>Stage (≥80 group)</b>						
I	1.00 (ref)			1.00 (ref)		
II	1.71 (1.15–2.55)			1.87 (0.95–3.67)		
III	2.51 (1.67–3.77)			4.89 (2.55–9.37)		
<b>Stage (&lt;80 group)</b>						
I	1.00 (ref)			1.00 (ref)		
II	2.58 (2.23–2.97)			3.82 (3.14–4.65)		
III	6.79 (5.89–7.82)			11.96 (9.87–14.48)		

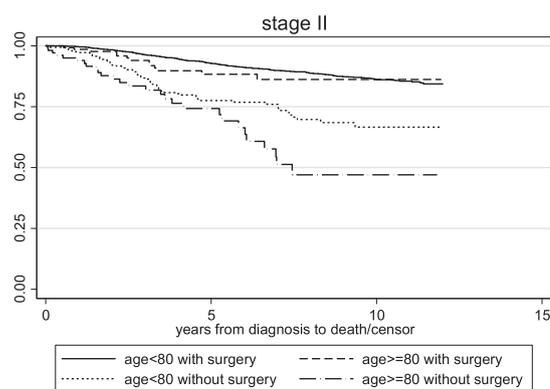
HR: Hazard Ratio, CI: Confidence Intervals.

Adjusted for age, ethnicity, other cancers, treatment, stage of cancer.

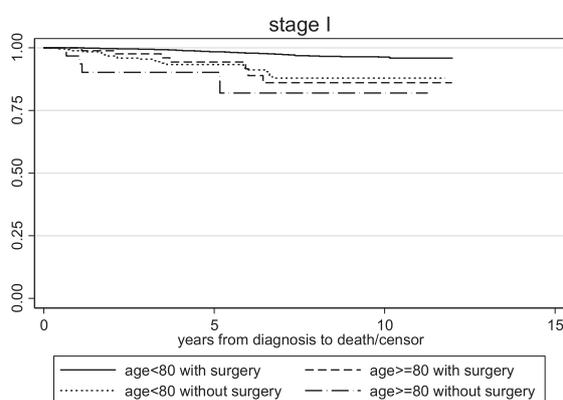
a. All patients, stages I-III



c. stage II



b. stage I



d. stage III

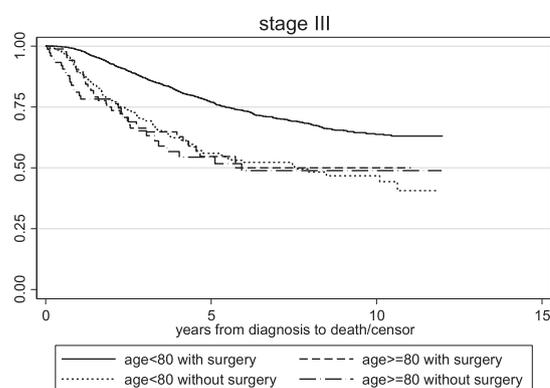


Fig. 1. Breast cancer specific survival by stage, age group and treatment received.

Elderly patients treated with surgery had improved OS and BCSS compared to those without surgery and those with no treatment, consistent across the stages of disease, even though this was statistically significant only for those with stage II disease (Tables 2 and 3, Fig. 1, a-d). Treatment with surgery yielded excellent outcomes with a 5-year BCSS at 96.1% compared to 99% in the younger counterpart for stage I disease (Fig. 1b); 92.1%–94.9% in stage II disease (Fig. 1c). These differences were statistically significant, but the absolute difference was small. In those with stage III disease, the elderly fared poorer compared to the younger patients in all the treatment groups (Table 2).

#### 4. Discussion

This study shows that extremely elderly women with breast cancer presented with more advanced disease and were treated less aggressively than their younger counterparts. Treatment with surgery for early breast cancer yielded good outcomes in the elderly with survival similar to that of younger patients, better than non-surgical treatment; and non-surgical treatment was better than no treatment. Surgery for the elderly with stage III disease yielded worse survival than in the younger group.

Our finding is similar to other reports where the elderly tend to present with later stage disease and received less treatment [8,11–13]. The International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA) [5] have recommended that patients 70 years or older should be

offered the same surgery as their younger counterparts. Despite this, treatment strategies for the very elderly group differ in different institutions across the world [14,15]. Bouchardy et al. concluded that suboptimal treatment was prescribed to half of the study population of 407 patients above 80 years of age resulted in an overall poorer prognosis [11]. In contrast, de Glas et al. found that omission of surgery did not alter the overall or relative survival amongst 26,292 patients in a Dutch breast cancer registry study [13]. However this studied the difference between groups of elderly patients all above 75 years of age, whereas our population study compared the very elderly with a much younger cohort, which had a median age of 53 years; this could possibly explain the different effect of surgery. Differences in stage distribution and tumor biology could also be contributory.

Among patients with early disease who had surgery, the elderly group did not fare worse than their younger counterparts, with 9 in 10 with stage I disease expected to survive beyond 5 years, with only 3% difference in BCSS. This difference widened with later stages. Surgery for breast cancer is safe for elderly women, especially for those with little or no comorbidities [9,16,17] and should be based on functional status and severity of comorbidities rather than chronological age [18]. Among those who are surgically fit, studies have shown that primary hormonal therapy should only be used for those with a short life expectancy of 2–3 years, beyond which, patients who had surgery had a significantly better outcome [19,20]. The Eastern Cooperative Oncology Group (ECOG) score and American Society of Anesthesiologists (ASA) score are examples of

tools that can help to distinguish overall fitness. Geriatric assessment tools [21] to further stratify elderly patients is likely more useful in making decisions for treatment.

Elderly patients with stage III disease had poorer survival. This may be due to less than optimal surgery for advanced disease where complex and radical surgery needed is less often performed, and reduced use of systemic adjuvant therapy. They were less likely to have adjuvant chemotherapy (2.9% v 53%) and radiotherapy (16.5% v 35.5%), but more likely to have hormonal therapy (55.2% v 42.8%). This was consistent with recommendations by the American Society of Clinical Oncology (ASCO) [22], where chemotherapy is recommended in the elderly if there is a 10-year survival benefit of at least 5%, and the use of multigene molecular assays be considered to estimate the risk of disease recurrence [23]. Adjuvant radiotherapy may be omitted in selected patients as it only conferred a small reduction in the 5-year local recurrence rate [24]. More elderly patients were given hormonal therapy probably due to more hormone-receptor positive cancers [23,25].

There were several limitations of this study. Patient functional status and comorbidities, details of breast and axillary surgery were not available to assess if the non-surgery option or suboptimal surgery was due to subjective physician assessments; Hormone receptor status of tumours was also unknown for correlation of hormonal therapy; Treatment was captured as a 'yes' and 'no' up to 6 months after the initial diagnosis; Sequential hormonal treatment after the sixth month may be under-reported; Details on completeness of adjuvant therapy, disease recurrence and its management were also not available.

Our study showed that patients 80 years and above with early breast cancer (stage I and II) can benefit from surgery, achieving good outcomes close to that of younger patients.

The decision to perform surgery in those with stage III disease should be personalised, taking into consideration the patient's biological age with risk stratification of their fitness to withstand the different treatment modalities. In managing those who are surgically unfit or choose not to have surgery, non-surgical treatment such as hormonal treatment for those with hormonal receptors and radiotherapy should be considered, as any treatment outperforms no treatment.

### Conflict of interest declaration

No conflict of interest to declare.

### Ethical approval

Ethical approval for this study was obtained from Singapore's Ministry of Health as well as the Institutional Review Board.

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