Original Article

Non-surgically treated older women with operable early breast cancer in Denmark

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ABSTRACT

INTRODUCTION: Women ≥ 70 years of age, especially women with co-morbidity, have not achieved the same increase in survival as younger women with early breast cancer. Older patients with and without co-morbidity do not receive primary surgical treatment as often as younger women do. The primary aim of this study was to describe older women with operable early breast cancer who are not surgically treated. Secondarily to evaluate if there is a need for further research to clarify if the women may potentially benefit from comprehensive geriatric care (CGC) according to receiving surgery.

METHODS: This was a descriptive cross-sectional study including 781 women ≥ 70 years of age with biopsy-verified early breast cancer in Denmark 2012-2017. Data were retrieved from the Danish Breast Cancer Cooperative Group registry and medical record reviews.

RESULTS: Women ≥ 70 years of age with early breast cancer who did not receive surgical treatment represent a group of frail patients with the characteristics of a geriatric population. Among older women with early breast cancer, 14% had no primary surgical treatment. CGC may identify relevant health issues and interventions that could increase the possibility of surgical treatment in this group of patients.

CONCLUSIONS: Women ≥ 70 years of age with early breast cancer who do not receive surgery represent a group of frail patients that may potentially benefit from special geriatric care. CGC may be a way to provide this special care. Further research is needed.

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Breast cancer is the most common cancer type among women [1]. The incidence of breast cancer has increased over the past 60 years and increases with age. Women ≥ 70 years of age account for one-third of new breast cancer cases [2]. More than 90% of the patients are diagnosed with early breast cancer stages I-II, for which the primary treatment, according to existing guidelines, is one-day surgery [1].

The prevalence of co-morbidity and frailty increases with age and potentially complicates the diagnostic process and treatment of breast cancer in older women [3]. Frailty may be defined as reduced physiological reserve and is an important predictor of surgical outcome [3, 4].].

More than 20% of women who are diagnosed with breast cancer have one or more co-morbidities [5, 6]. Within the past 10-15 years, the general survival of breast cancer patients has improved. However, women ≥ 70 years of

age, especially women with co-morbidity, have not achieved the same increase in survival as younger women with breast cancer [1]. Older women with co-morbidity and cancer are often excluded from randomised studies. There is a general lack of knowledge about this group of patients.

Women ≥ 70 years of age with early breast cancer constitute a heterogeneous group [7]. In general, older women with or without frailty respond well to surgical treatment of early breast cancer and few perioperative complications are observed [8]. However, it has been shown that older women, both with and without co-morbidity, do not receive breast cancer treatment according to guidelines as often as younger women [6, 9]. .

The Danish national guidelines for breast cancer treatment were updated in 2009 by the Danish Breast Cancer Cooperative Group (DBCG). The update included a specific guideline for older patients and patients with co-morbidity who have a newly diagnosed and operable early breast cancer. According to these guidelines, only patients with a life expectancy below two years or patients assessed as unfit for surgery should not be offered surgery [1, 10, 11]..

Many factors impact the decision about whether a woman is fit for surgery or not, e.g., co-morbidity burden, polypharmacy, mental capacity, psychical performance and nutrition status. Together, these parameters describe how fit or frail a woman is. Frailty may be assessed and used in risk stratification, but it can also potentially be modified by the right intervention [4, 12]. Comprehensive geriatric care (CGC) of older patients encompasses geriatric assessment and intervention in various domains by a multidisciplinary team. CGC ensures that all relevant issues related to co-morbidity, polypharmacy, psychological, cognitive and functional level, nutrition and social network are identified, quantified and managed.

Factors influencing the decision to perform primary surgery in older women with operable early breast cancer remain unknown. Thus, it is not known if women ≥ 70 years of age who do not receive primary surgical treatment would be capable of receiving surgery if managed with CGC.

The primary aim of this study was to describe women who were not surgically treated for operable early breast cancer. The secondary aim was to evaluate if there is a basis for further research to explore if any benefit may be reaped from CGC according to receiving surgery.

METHODS

Design

This was a descriptive cross-sectional study based on data from Danish national clinical databases and review of electronic medical records.

Setting and study population

The study included a total of 781 patients registered in DBCG registry with early breast cancer stages I-II and an age ≥ 70 years who had been diagnosed at Aarhus University Hospital or Randers Regional Hospital, Denmark, in the period from 1 January 2012 to 1 October 2017. Data from the DBCG registry included tumour characteristics, age at diagnosis, hospital and primary therapy. Data from the retrospective reviews of the electronic medical record included co-morbidity burden, medications, functional capacity, home care, social circumstances and the decision about surgery (**Table 1** and **Table 2**). Medical record review was performed retrospectively in 109 women registered with operable early breast cancer in the DBCG register without surgical treatment to characterise patients who did not receive surgery, but also in all women ≥ 85 years of age who had undergone surgery to compare baseline characteristics in the oldest patients receiving and not receiving surgery.

The review was performed by a specialist in geriatric medicine. The assessment of whether a patient would

potentially benefit from geriatric involvement was based on a clinical assessment by the experienced specialist based on the data collected.

TABLE 1 / Baseline characteristics of all women ≥ 70 years with early breast cancer.

	Undergoing surgery (N$_s$ = 672)	Not undergoing surgery (N$_n$ = 109)	Total (N$_{tot}$ = 781)	p-value
Age at diagnosis[a], yrs, median (IQR) [range]	76 (73-80) [70-92]	85 (82-88) [70-98]	77 (73-82) [70-98]	⟨ 0.001
Age groups, n (%) [row%]				
70-74 yrs,	270 (40) [99]	4 (4) [1]	274 (35) [100]	
75-79 yrs	221 (33) [94]	15 (14) [6]	236 (30) [100]	
80-84 yrs	138 (20) [81]	33 (30) [19]	171 (22) [100]	
85-89 yrs	38 (6) [51]	36 (33) [49]	74 (10) [100]	
≥ 90 yrs	5 (1) [19]	21 (19) [81]	26 (3) [100]	
Oestrogen receptor, n (%)				0.001
Positive	610 (91)	109 (100)	719 (92)	
Negative	62 (9)	0	62 (8)	
HER2 receptor, n (%)				0.306
Positive	77 (11)	2 (2)	79 (10)	
Negative	569 (85)	31 (28)	600 (77)	
Unknown	26 (4)	76 (70)	102 (13)	
Tumour size, n (%) [row%]				⟨ 0.001
⟨ 20 mm	317 (47) [93]	24 (22) [7]	341 (44) [100]	
20-50 mm	330 (49) [80]	82 (75) [20]	412 (53) [100]	
Unknown	25 (4) [89]	3 (3) [11]	28 (3) [100]	
Hospital, n (%) [row%]				0.276
Aarhus	431 (64) [87]	64 (59) [13]	495 (63) [100]	
Randers	241 (36) [84]	45 (41) [16]	286 (37) [100]	
Calendar year of diagnosis, n (%) [row%]				0.199
2012	102 (15) [89]	12 (11) [11]	114 (15) [100)]	
2013	113 (17) [81]	26 (24) [19]	139 (18) [100]	
2014	89 (13) [86]	14 (13) [14]	103 (13) [100]	
2015	109 (16) [82]	24 (22) [18]	133 (17) [100]	
2016	127 (19) [89]	16 (14) [11]	143 (18) [100]	
2017	132 (20) [89]	17 (16) [11]	149 (19) [100]	
Type of primary therapy, n (%)				⟨ 0.001
Mastectomy	276 (41)	0	276 (35)	
Lumpectomy	377 (56)	0	377 (48)	
Lumpectomy + mastectomy	19 (3)	0	19 (2)	
Biopsy only	0	109 (100)	109 (14)	

HER2 = human epidermal growth factor receptor 2; IQR = interquartile range.
a) Age at date of biopsy.

TABLE 2 / Aged-stratified characteristics of women ≥ 70 years with early breast cancer not undergoing surgery.

	Age groups				
	old: 70-79 yrs (N = 19)	old-old: 80-89 yrs (N = 69)	oldest-old: ≥ 90 yrs (N = 21)	total: 70-98 yrs (N = 109)	p-value
Co-morbidity, CIRS-G, n (%) [row%]					0.142
Low	1 (5) [6]	11 (16) [69]	4 (19) [25]	16 (15) [100]	
Moderate	11 (58) [17]	41 (59) [61]	15 (71) [22]	67 (61) [100]	
Severe	7 (37) [27]	17 (25) [65]	2 (10) [8]	26 (24) [100]	
Prescription drugs, n, mean ± SD (range)	8 ± 3.6 (1-15)	6 ± 4.4 (0-19)	6 ± 3.9 (0-17)	6 ± 4 (0-19)	0.391
Housing, n (%) [row%]t					0.035
Own home	17 (89) [19]	60 (87) [67]	12 (63) [14]	89 (81) [100]	
Nursing home	2 (11) [11]	9 (13) [50]	7 (37) [39]	18 (17) [100]	
Unknown				2 (2)	
Living alone, n (%) [row%]					0.500
Yes	9 (47) [14]	43 (62) [68]	11 (58) [18]	63 (58) [100]	
No	10 (53) [23]	26 (38) [59]	8 (42) [18]	44 (40) [100]	
Unknown				2 (2)	
Walking device, n (%) [row%]					0.018
Yes	6 (33) [10]	41 (60) [66]	15 (79) [24]	62 (57) [100]	
No	12 (67) [28]	27 (40) [63]	4 (21) [9]	43 (39) [100]	
Unknown				4 (4)	
Home care n (%) [row%]:					0.385
Yes	10 (53) [15]	41 (59) [63]	14 (74) [22]	65 (60)	
No	9 (47) [21]	28 (41) [67]	5 (26) [12]	42 (38)	
Unknown				2 (2)	
Practical, n (%) (N = 65):					-
Yes	9 (100)	41 (100)	14 (100)	64 (99)	
No	-	-	-	0	
Unknown	-	-	-	1 (1)	
Personal, n (%) (N = 65):					0.663
Yes	7 (78)	27 (66)	11 (79)	45 (69)	
No	2 (22)	14 (34)	3 (21)	19 (29)	
Unknown	-	-	-	1 (2)	
Relatives represented at consultation with surgeon, n (%) [row%]					0.053
Yes	10 (56) [13]	49 (79) [65]	16 (89) [21]	75 (69) [100]	
No	8 (44) [35]	13 (21) [56]	2 (11) [9]	23 (21) [100]	
Unknown	-	-	-	11 (10)	
Type of relatives:					
Spouse/partner	0	8	0	8	
Children	7	36	13	56	
Daughter/son-in-law	1	1	1	3	
Grandchildren	1	1	2	4	
Friend	2	2	0	4	
Other	0	5	2	7	
Decision of no surgery, n (%) [row%]					0.791
Surgeon	8 (42) [16]	34 (49) [67]	9 (43) [18]	51 (42) [100]	
Patient	11 (58) [19]	35 (51) [60]	12 (57) [21]	58 (58) [100]	
CGC may facilitate surgery n (%) [row%]:					0.516
Yes	16 (84) [19]	55 (80) [64]	15 (71) [17]	86 (79) [100]	
No	3 (16) [13]	14 (20) [61]	6 (29) [26]	23 (21) [100]	
Surgeon decided no surgery, n (% of 51) (N = 51)	6	24	5	35 (69)	
Patients decided no surgery, n (% of 58) (N = 58)	10	31	10	51 (89)	

CGC = comprehensive geriatric care; CIRS-G = Cumulative Illness Rating Scale-Geriatric; SD = standard deviation.

Statistical analyses

Descriptive statistic baseline data for categorical variables were calculated as percentages. Continuous variables were calculated using mean with standard deviations for normally distributed data and median, interquartile range and range for non-normally distributed data.

Categorical variables were analysed using the Pearson's chi-squared test or Fisher's exact test. Continuous variables were analysed using Student's t-test for parametric variables and the Wilcoxon's rank sum test for non-

parametric variables. A p-value < 0.05 was considered statistically significant. Statistical analyses were done.

Trial registration: not relevant.

RESULTS

Data on 836 women were received from the DBCG registry. A total of 55 women were excluded due to advanced disease or because they had been diagnosed before January 2012.

In the study period, 781 patients ≥ 70 years of age with biopsy-verified early breast cancer stages I-II were seen in the breast cancer clinic at the two hospitals. A total of 109 (14%) did not undergo primary surgery (Table 1).

The median age among women not undergoing surgery and women undergoing surgery was 85 years and 76 years, respectively. In the non-surgically treated group, no women were oestrogen negative, whereas 62 of 672 women undergoing surgery were oestrogen negative. There was no difference between the groups in calendar year of diagnoses or probability of receiving surgery (Table 1).

Women without surgery were stratified into three age categories, with the majority of women aged 80-89 years. All women had some degree of co-morbidity - most often moderate. There were no differences in co-morbidity score between age categories.

Most of the women lived alone (58%), used a walking device (62%) and received help for practical (99%) and personal (69%) care in their home. 17% lived in a nursing home.

In the first consultations with the surgeon, most women were accompanied by relatives regardless of age; most often children, subsequently by their spouse or partner. The decision not to perform surgery was made by the surgeon in 42% of the cases.

The geriatric specialist who performed the medical record review assessed that CGC could potentially identify relevant health issues and interventions in 79% of the patients (Table 2).

Surgically versus non-surgically treated women were compared in a subgroup of all women ≥ 85 years of age. In general, women not undergoing surgery were older, had more co-morbidity and received more personal home care than women who underwent surgery. The proportion of women accompanied by relatives did not differ in the groups, but the kind of support by relatives may have differed. Very few women seemed to have a healthy partner who was actually able to support them during their illness (**https://ugeskriftet.dk/files/a04200226_supplementary.pdf**) (**Table 3**).

TABLE 3 / Characteristics of women ≥ 85 years with early breast cancer undergoing and not undergoing surgery.

	Undergoing surgery (N$_s$ = 43)	Not undergoing surgery (N$_n$ = 57)	Total (N$_{tot}$ = 100)	p-value
Age at diagnosis, yrs, median (IQR) [range]	86 (86-88), 85-92	88 (86-91), 85-98	87 (86-90), 85-98	0.023
Co-morbidity, CIRS-G, n (%) [row%]				0.046
Low	16 (37) [64]	9 (16) [36]	25 (25) [100]	
Moderate	23 (54) [37]	39 (68) [63]	62 (62) [100]	
Severe	4 (9) [31]	9 (16) [69]	13 (13) [100]	
Prescription drugs, n, mean ± SD (range)	6 ± 3.6 (0-13)	6 ± 3.8 (0-17)	6 ± 3.7 (0-17)	0.735
Housing, n (%) [row%]				0.006
Own home	42 (98) [48]	45 (79) [52]	87 (87) [100]	
Nursing home	1 (2) [8]	12 (21) [92]	13 (13) [100]	
Living alone, n (%) [row%]				0.017
Yes	36 (83) [51]	34 (62) [49]	70 (70) [100]	
No	7 (16) [25]	21 (38) [75]	28 (28) [100]	
Unknown	-	-	2 (2) [100]	
Walking device, n (%) [row%]				0.019
Yes	16 (37) [33]	33 (61) [67]	49 (49) [100]	
No	27 (63) [56]	21 (39) [44]	48 (48) [100]	
Unknown	-	-	3 (3)	
Home care n (%) [row%]:				0.921
Yes	27 (63) [44]	34 (62) [56]	61 (61) [100]	
No	16 (37) [43]	21 (38) [57]	37 (37) [100]	
Unknown	-	-	2 (2)	
Practical, n (%) (N = 61):				-
Yes	34 (100)	27 (100)	61 (100)	
No	-	-	-	
Personal, n (% of 61) (N = 61):				⟨ 0.001
Yes	4 (15)	24 (71)	28 (46)	
No	23 (85)	10 (29)	33 (54)	
Relatives represented at consultation with surgeon, n (%) [row%]				0.974
Yes	35 (81) [45]	43 (81) [55]	78 (78) [100]	
No	8 (19) [44]	10 (19) [56]	18 (18) [100]	
Unknown	-	-	4 (4)	

CIRS-G = Cumulative Illness Rating Scale-Geriatric; IQR = interquartile range; SD = standard deviation.

DISCUSSION

In this cohort of 781 patients, surgery was not the primary treatment in 14% of patients, which is similar to results from a previous study [9]. Recent years' focus on older women with breast cancer does not seem to have changed the attitude towards surgical treatment in this group of older patients; we found no change in the number of non-surgically treated patients between 2012 and 2017. This may indicate a need for a new approach to older patients with early breast cancer.

In accordance with other studies [9, 13], our results showed that non-surgically treated patients have a higher median age than patients undergoing surgery [13]. Among women ≥ 85 years of age, we observed that estrogen receptor negative patients were more likely to receive surgery despite having a moderate to severe level of co-morbidity.

All patients not undergoing surgery had a positive oestrogen receptor level, possibly indicating that the decision to abstain from surgery is more appealing to both the surgeon and the patient as endocrine therapy is a part of recommended adjuvant treatment in addition to surgery according to guidelines [10, 14].

We used the Cumulative Illness Rating Scale-Geriatric [15] to assess co-morbidity as this tool measures the chronic illness burden more specifically than, e.g., the Charlson's Comorbidity Index [16]. In the group of patients ≥ 85 years of age, patients not undergoing surgery had a higher co-morbidity burden than patients undergoing surgery, which is in accordance with the findings made in other studies [6]. All patients not undergoing surgery had some degree of co-morbidity [13, 17]. This underlines that co-morbidity influences the choice of treatment. Only one-fifth of the non-surgically treated women had severe co-morbidity, which indicates that co-morbidity cannot or should not be the sole reason for not having surgery.

In approximately 75% of the consultations with the surgeon, relatives were represented. The spouse/partner was often not represented at the consultation, indicating that the partner was not a resource in the treatment process. In some cases, the decision not to have surgery was made by the patient because she had a partner at home to take care of (**https://ugeskriftet.dk/files/a04200226_supplementary.pdf**). Among the oldest patients undergoing surgery, the accompanying relatives were more often able to support the women in the process as opposed to the relatives of non-surgically treated patients. This may indicate that the choice of treatment was also influenced by the patients' social network.

We know that women ≥ 70 years of age with early breast cancer are a heterogeneous group [7]. Our results suggest that patients not undergoing surgery differ from same-age counterparts who do receive surgery. They have a higher co-morbidity burden, a higher need for support in daily living, are less supported by relatives and they more often use a walking device and have polypharmacy - all of which describe a frail group of patients with a potential need of special care.

This study has several limitations that need to be considered when interpreting the results. Lack of information in the electronic medical record can lead to false conclusions. Also, only one geriatric specialist performed the clinical assessment and it was based on clinical experience. The clinical assessment can be used only as guidance for the need of further research, and it is not a sufficient geriatric assessment based on validated tools like it would be in a randomised study. Furthermore, the groups were relatively small and data potentially restricted by selection bias and residual confounding due to incomplete data about, e.g., medical treatment compliance, misclassification of data and retrospectively collected data from medical records.

It is known that older patients with early breast cancer and co-morbidity do not undergo surgery as often as patients without co-morbidity [6, 9]. This study further suggests that patients who do not undergo surgery represent a group of frail patients. From the literature we do not know whether the group of non-surgically treated patients could be fit for surgery, and we do not know exactly which assessment and intervention may facilitate surgery. Also, more knowledge is needed to address if patients would accept an optimising intervention, and if such interventions would change the treatment preference, both from a patient and a surgeon perspective. In this study, CGC could potentially identify relevant health issues and interventions in 79% of the patients; and if patients accepted suggested interventions, this would potentially lead to surgical treatment. The existing guidelines recommend surgical treatment of operable early breast cancer when life expectancy exceeds two years and the patient is assessed fit for surgery. There are clear indications in the literature that CGC can improve compliance, treatment tolerability, quality of life and survival in frail older patients with early breast cancer [10, 18]. It is also well-known that there is a need for and a benefit from having a multidisciplinary, perioperative team including geriatricians to take care of older frail patients in relation to elective surgery [18-20]. Geriatric care is described in the updated recommendation for older breast cancer patients of International Society of Geriatric Oncology and the European Society of breast Cancer Specialists [10].

CONCLUSIONS

Women ≥ 70 years of age with early breast cancer who did not receive primary surgical treatment represent a group of frail patients with the characteristics of a geriatric population. A retrospective geriatric review identified multiple health issues in 79% of the patients indicating that this group of patients would probably benefit from CGC, which may potentially optimise their treatment trajectory and facilitate surgery. Future research is needed to investigate whether CGC may facilitate surgery in patients initially not receiving surgery for early breast cancer.

Ethics

This study was approved by the Danish Data Protection Agency (record number 1-16-02-833-17), the Danish Patient Safety Authority (record number 3-3013-2358/1) and by chief physicians at the Department of Plastic Surgery, Aarhus University Hospital and Centre for Breast Surgery, Randers Regional Hospital allowing review of medical records. The Danish Clinical Registries provided data from the DBCG registry. Data were stored in RedCap, Aarhus University.

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LITERATURE

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