Decision making in geriatric oncology
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Chapter 2
Trends in breast cancer treatment in the elderly at a breast cancer outpatient clinic


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A translation of: “Trends in de behandeling van borstkanker bij ouderen op een mammapolikliniek: minder vaak operatieve behandeling”
Abstract

Aim: To assess the treatment of elderly patients with resectable breast cancer treated at the Medical Centre Alkmaar before and after the implementation of a multidisciplinary breast cancer team in February 2006.

Methods: Retrospective chart review of all patients aged 70 years and older with a newly diagnosed resectable breast tumour (stage I and II) treated between 2002 and 2007.

Results: Of 232 patients, 84% received surgical treatment. Adjuvant treatment with radiotherapy, endocrine therapy and chemotherapy was given to 88, 91 and 5 patients respectively. Over time, there was a significant decrease in the percentage of patients that were treated surgically, particularly for patients aged 80 years and older. The number of patients receiving radiotherapy in accordance with guidelines improved over time, while the guideline adherence for endocrine treatment remained more or less stable. The reporting of decisions regarding treatment and guideline discordance improved.

Conclusion: Between 2002 and 2007, treating physicians seemed more aware of guidelines and guideline discordance was more clearly motivated in the patient’s chart. Guideline adherence for radiotherapy improved but there was a significant decrease in surgical treatment over time, particularly in patients aged 80 years and older.
Introduction
In the coming decades, increasing life expectancy and ageing of the population will result in a substantial increase in the number of older cancer patients; it is expected that by 2035, 60% of all new breast cancer patients will be over 70 years of age. Although attempts have been made to actively include older patients in oncologic trials, most treatment guidelines are still based on research done in relatively fit patients. In addition, changes in tumour characteristics with increasing age have important prognostic and therapeutic implications. Furthermore, comorbidity, polypharmacy, decreased functional capacity and decreased physiological reserve result in increasing heterogeneity in the elderly population; these factors must be taken into account in the decision-making process.

Previous studies have shown that case review by a multidisciplinary breast cancer team at a breast cancer clinic resulted in an alteration of the treatment for over 50% of patients. Furthermore, pre-operative consultation with an oncologist has been shown to result in better guideline adherence for breast cancer patients.

In the Netherlands, decision making for breast cancer treatment is increasingly done in a multidisciplinary breast cancer team (MBCT), which includes treating physicians (surgeons, oncologists, radiotherapists), supporting specialists (pathologists, radiologists) and specialised nurses. These MBCTs have been developed by the Integral Cancer Centres (IKC) and their procedures have been recorded in the “Organization of Breast Cancer Care” written by the National Breast Cancer Council Netherlands (NABON).

In February 2006, a weekly MBCT meeting was initiated at the Medical Centre Alkmaar in the Netherlands. In this study, we examined if the implementation of this MBCT influenced treatment decisions and guideline adherence for older patients with a resectable breast cancer treated at the breast cancer out-patient clinic of this hospital.

Methods
We performed a retrospective cohort study of patients aged 70 years and older, treated at the Medical Centre Alkmaar, in the Netherlands, for a newly diagnosed, primary resectable breast cancer (stage I or II) between January 2002 and December 2007. Patients with a second primary breast cancer, involvement of a fixed parasternal (N2), subclavicular or supraclavicular lymph node (N3) or distant metastases (M1) were excluded.

The following variables were collected from the patient’s medical and surgical charts, and pathology reports: age, date of diagnosis, histological data, tumour grade, mitotic activity, stage (TNM), oestrogen and progesterone receptor status, expression of human epidermal growth factor type 2 (Her2Neu), as well as data on the initial treatment. The stage of
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disease was subdivided into two categories: stage I (T1N0M0) and stage II (T0-2N1M0 or T3N0M0).
The presence of the following comorbid diseases was recorded: valvular disease, angina pectoris, myocardial infarction, heart failure, arrhythmias, left ventricular hypertrophy, hypertension, diabetes, stroke, Parkinson’s disease, pulmonary embolism, chronic obstructive lung disease, rheumatoid arthritis, renal insufficiency, prior malignancies, osteoporosis, thyroid disease, dementia, mood disorders, psychotic disorders and personality disorders.
The actual diagnostic process and initial treatment were compared to the national guidelines, as developed by the NABON.\textsuperscript{15,16} Table 1 lists an overview of the recommendations for diagnosis and treatment for patients aged 70 years and over during the study period.
In case of discordance with guidelines, the patient’s chart was consulted to find the motivation behind these treatment choices.

\begin{table}
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Indication} & \\
\hline
\textbf{Diagnostic procedures} & \\
\hline
Histology & Breast cancer should be histologically confirmed in all patients. \\
Lymph node status & In case of surgical treatment, a diagnostic procedure for assessing lymph node status is required. \\
\hline
\textbf{Treatment} & \\
\hline
Surgery & Surgery is indicated in all patients with stage I and II disease. \\
Radiotherapy & 1. Radiotherapy is always required after breast conserving treatment.  
2. Locoregional radiotherapy is also required in case of irradical mastectomy. \\
Endocrine therapy & \\
Jan 2002 to Sept 2005 & 1. In case of hormone receptor negative breast cancer, endocrine treatment is not required.  
2. In the absence of lymph node metastases and in case of hormone receptor positive disease, endocrine treatment is recommended if:  
a. tumour is larger than 3 cm  
b. tumour size is between 1 and 3 cm and mitotic activity is greater than 10  
3. In case of lymph node metastases and hormone receptor positive disease, endocrine treatment is always required. \\
Endocrine therapy & \\
Oct 2005 to Dec 2007 & 1. As in Jan 2002 to Sept 2005  
2. In the absence of lymph node metastases and in case of hormone receptor positive disease, endocrine treatment is recommended if:  
a. tumour is larger than 1 cm and grade III disease  
b. tumour is larger than 2 cm and grade II-III  
c. tumour is larger than 3 cm  
3. As in Jan 2002 to Sept 2005 \\
Chemotherapy & There are no strict recommendations for chemotherapy in patients aged 70 years or older. Chemotherapy should be considered for patients with hormone receptor negative disease and a high risk of recurrence. \\
\hline
\end{tabular}
\caption{Diagnostic and treatment guidelines for stage I and II breast cancer in patients aged 70 years and older\textsuperscript{15,16}}
\end{table}
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**Statistical analysis**

To assess differences between age groups and differences in guideline adherence between various subgroups, the SPSS (Statistical Package for the Social Sciences) version 14.0 was used. The chi-square test was used for nominal and ordinal variables. For continuous variables with a normal distribution, the Student t-test was used, and for continuous variables with a non-normal distribution the Mann-Whitney test.

**Results**

**Patient and tumour characteristics**

Between January 2002 and December 2007, 285 patients aged 70 years and older presented with a resectable breast cancer at our clinic. After exclusion of 53 patients with a second primary breast cancer, 232 patients (229 women, 3 men) remained for further analysis. Median age of these patients was 77.9 years (range 70-94 years; Table 2). For 102 patients, disease was at stage I (44%), and for 120 at stage II (56%).

For the great majority of patients, the presence of breast cancer was histologically confirmed (n=227, 98%). Hormone receptor status was assessed in 220 patients (95%); 86% (189/220) was oestrogen receptor positive and 74% (163/220) was progesterone receptor positive. Her2Neu status was assessed in 84 patients, and an overexpression of these receptors was found in seven patients (8.3%).

Over time, no significant changes were seen in the stage of disease at presentation or the tumour characteristics.

Data on comorbidity was available for 230 patients; 68 had no concurrent disease (30%). The most frequent comorbid conditions were cardiac arrhythmias (n=33), angina pectoris or myocardial infarction (n=40), hypertension (n=81), diabetes (n=32), heart failure (n=11), stroke (n=22), pulmonary disease (n=13), psychiatric disorders and dementia (n=19) and a prior malignancy (n=18). Comorbidity increased over time; in 2002, 19% of patients had three or more comorbid conditions, which increased to 33% by 2007 (p=0.059).

Table 2: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>2002-3</th>
<th>2004-5</th>
<th>2006-7</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>232</td>
<td>71</td>
<td>75</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Median age</td>
<td>75.9 years</td>
<td>76.8 years</td>
<td>78.4 years</td>
<td>78.3 years</td>
<td>0.178</td>
</tr>
<tr>
<td>Stage I</td>
<td>102 (44%)</td>
<td>33 (46%)</td>
<td>31 (41%)</td>
<td>38 (44%)</td>
<td>ns</td>
</tr>
<tr>
<td>Stage II</td>
<td>130 (56%)</td>
<td>38 (54%)</td>
<td>44 (59%)</td>
<td>48 (56%)</td>
<td>ns</td>
</tr>
<tr>
<td>Oestrogen receptor positive</td>
<td>189/220 (86%)</td>
<td>55/67 (82%)</td>
<td>65/74 (88%)</td>
<td>76/86 (88%)</td>
<td>ns</td>
</tr>
<tr>
<td>Progesterone receptor positive</td>
<td>163/220 (74%)</td>
<td>48/67 (71%)</td>
<td>55/73 (75%)</td>
<td>65/86 (75%)</td>
<td>ns</td>
</tr>
<tr>
<td>Her2neu overexpression</td>
<td>7/84 (8%)</td>
<td>0/0 (-)</td>
<td>4/25 (16%)</td>
<td>3/59 (5%)</td>
<td>ns</td>
</tr>
<tr>
<td>Number of comorbid disease</td>
<td>1.5</td>
<td>1.3</td>
<td>1.4</td>
<td>1.8</td>
<td>0.059</td>
</tr>
</tbody>
</table>

*ns = not significant
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**Treatment**

Overall, 195 patients received surgical treatment (84%); 109 had a modified radical mastectomy and 86 patients had breast conserving surgery. In 192 of the 195 patients treated surgically, an additional procedure for staging of the axillary nodes was performed; for 128 of these, a sentinel node procedure was used.

Of the 86 patients with breast conserving surgery, 80 received adjuvant radiotherapy (93%) in accordance with guidelines. Radiation after a modified radical mastectomy was recommended by guidelines for nine patients, and eight were treated accordingly (88%). Adjuvant hormonal treatment was recommended for 103 patients, and was given to 91 of these (88%). In addition, five patients received adjuvant chemotherapy due to irradical surgery, high risk disease or lymph node metastases.

Despite resectable disease, surgery was withheld in 37 patients (13 with stage I disease, 24 with stage II). These patients were significantly older (median age 86.1 years vs. 76.3 years in patients treated surgically, p<0.001) and had significantly more comorbidity (median number of disease 2.43 vs. 1.33 in patients treated surgically, p<0.001). For one patient, no treatment was given and for two patients, treatment was unclear. The remaining 34 patients received primary endocrine treatment (tamoxifen n=21, anastrozole n=13). Two patients eventually did receive a modified radical mastectomy, one due to disease progression after 10 months of endocrine treatment, and one due to an alteration in the patient’s wishes 11 months after diagnosis. At the end of the study period, after a median follow-up of 1.9 years, 14 of these 37 patients had stable disease, three had progressive or metastatic disease and 13 patients had died. Cause of death was generally not available. A further seven patients were lost to follow-up.

Figure 1 shows the changes in guideline adherence over time. The use of endocrine treatment and chemotherapy remained more or less the same, while the use of radiotherapy increased (2002-2003 85%, 2004-2005 97%, 2006-2007 100%, p=0.03). There was a significant decrease in guideline adherence for surgical treatment: in the first two years 94% of patients with stage I and II were treated surgically, but this decreased to 84% in 2004-2005 and was as low as 76% in 2006-2007 (p=0.002). This decrease was particularly evident in patients aged 80 years and over, for whom guideline adherence decreased from 80% in 2002-2003 to 33% in 2006-2007 (p=0.01); in the same time period, the percentage of patients aged 70-80 years that received surgical treatment, as recommended by guidelines, remained over 95%.

**Guideline adherence and the MBCT**

Overall, 170 of the 232 patients were diagnosed and treated in accordance with national guidelines (77%). Over time, a non-significant decrease in guideline adherence was seen: 83% of patients (59/71) in 2002-2003, 77% (58/75) in 2004-2005, and 74% (62/85) in
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2006-2007 (p=0.23). As demonstrated by Figure 1, this decrease was primarily due to the decrease in the percentage of patients treated surgically. Reporting of reasons behind guideline discordance improved over time: in 2002-2003 this decision was motivated in 22% of patients (2/9), in 2004-2005 in 93% (12/13) and in 2006-2007 in 100% (21/21, p<0.001). Of the 35 documented decisions not to follow guidelines, 19 were due to comorbidity (42%) including previous malignancy (n=3), cardiac disease (n=5), dementia (n=1), depression (n=3) and stroke (n=4). Other documented reasons for guideline discordance were the patient’s overall condition (n=4, 9%), age (n=5, 13%) or the patient’s preference (n=14, 35%).

The weekly MBCT conference at the Medical Centre Alkmaar was initiated in February 2006. In the first year, 82% of newly diagnosed patients were discussed at this conference; this percentage increased to 98% in 2007. Although a direct comparison of treatment before and after the start of the MBCT conference does show significant differences in guideline adherence, Figure 1 shows that these are due to trends that were already visible in the years before the MBCT meetings were initiated. This makes causal relationship between the start of the MBCT conferences and these developments unlikely.

**Figure 1: Treatment patterns per two year interval**

![Chart showing trends in breast cancer treatment](chart.png)

*Surg=surgery, Ax=surgical procedure for axillary lymph node staging, RT=radiotherapy, ET=endocrine therapy, CT=chemotherapy*

Percentages represent the amount of patients for whom a specific treatment was recommended that actually receiving this treatment. For chemotherapy, this percentage represents the number of patients for whom chemotherapy should have been considered that actually received chemotherapy. The multidisciplinary breast cancer team meetings started in February 2006.
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Discussion
In this study, we assessed changes in the treatment of resectable breast cancer in patients aged 70 years and older in a large peripheral Dutch hospital between 2002 and 2007. Over time, the use of endocrine treatment and chemotherapy remained stable, and an increase was seen in the use of adjuvant radiotherapy. However, we found a significant decrease in the number of patients treated surgically, particularly in patients aged 80 years and older, for whom adherence to surgical guidelines decreased from 80 to 33% over time. These patients were older and had more comorbidity than surgically treated patients, and often received primary endocrine therapy instead. Interestingly, we also found an increase in the number of comorbid conditions for the entire patient group. This trend has been seen in other studies.\textsuperscript{17,18}

Breast cancer surgery in itself has a low mortality risk (0.0-0.3%).\textsuperscript{1,10} However, previous studies have demonstrated that comorbid conditions are the primary cause of post-operative complications and mortality.\textsuperscript{19} Furthermore, 10% of older patients experience a post-operative decrease in cognitive function.\textsuperscript{20} In addition, multiple studies have shown that comorbidity plays a greater role in overall survival than cancer-specific mortality, particularly in case of early stage disease.\textsuperscript{1,10,11,21} This is also demonstrated by a recent Cochrane review, on breast cancer in women aged 70 years and older,\textsuperscript{22} which found no difference in overall survival between patients receiving surgical treatment only when compared to endocrine monotherapy. Limited life-expectancy due to comorbidity could therefore be a legitimate reason to withhold surgery. However, progressive disease can have a significant impact on quality of life; the same Cochrane review demonstrated that primary endocrine treatment results in a significant decrease in progression-free survival.\textsuperscript{22}

We found that between 2002 and 2007 treating physicians seemed to be more aware of guidelines as guideline discordance was more frequently motivated in the patient’s chart: in 2002-2003 only 22% of these decisions were motivated in the chart compared to 100% in 2006-2007 (p<0.001). Comorbidity (in 42%) and patient’s preference (in 35%) were the primary reasons to adjust treatment.

Although assessing for differences between treatment before and after the implementation of the weekly MBCT conference reveals some differences, these are based on trends already visible before the start of the MBCT meetings (Figure 1). The implementation of these conferences thus seems to be a part of a greater awareness of the importance of adequate treatment for older patient with breast cancer, and a recognition of the complexity of treatment decisions, requiring a multidisciplinary approach. This fact has also been stressed in a recent report by the Dutch Health Care Inspection (IGZ) on coordinated care trajectories for cancer patients, addressing the
importance of multidisciplinary treatment and collaboration of the different specialists involved in the treatment process.\textsuperscript{23}

In conclusion, between 2002 and 2007, we found an increased awareness of treatment guidelines among the treating physicians involved in the treatment of breast cancer; treatment decisions were better motivated. For older patients, guidelines on adjuvant radiotherapy were followed more frequently, but we found a significant decrease in the use of surgical treatment, particularly in patients aged 80 years and older. Comorbidity and patient’s preference were of primary importance for guideline discordance. Well-coordinated multidisciplinary treatment remains of the utmost importance, particularly in older cancer patients.
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References