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Locoregional control and survival after breast conserving therapy

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Background. *The purpose of our study was to present a 5-year survival and locoregional control rates in breast cancer patients and to establish eventual impact of the treatment and patient characteristics on locoregional control and survival.*

Methods. *From January 1998 to December 1999 564 stage 1 and 2 breast cancer patients were treated with breast conserving therapy. We evaluated the following characteristics: age, histological diagnosis, grade, size, number of metastatic lymph nodes, hormonal receptor status, extensive intraductal component (EIDC), vascular invasion, pathologic tumour margins, type of surgery and use of adjuvant therapy.*

Results. *The mean age of our patients was 54.2 years. Invasive ductal carcinoma was the most common diagnosis (82.4%), followed by invasive lobular carcinoma (10.6%). Most of the tumours were grade 2. Seventy-two % of patients had T1 tumours, 24% T2 and 3% T_{is} tumours. Metastatic lymph nodes were present in 44% of patients. All patients were treated with breast conserving surgery followed by radiotherapy (RT). Fifty % of patients received adjuvant chemotherapy and/ or hormonal therapy. The 5-year survival rate was 88.5%. Tumour size, number of metastatic lymph nodes, grade, hormonal receptors and vascular invasion proved to be statistically significant prognostic factors for the survival, while age and histological diagnosis were not. Local recurrence developed in 4.3% of our patients, while in 3.4% regional recurrence developed.*

Conclusions*. Breast conserving surgery followed by RT was associated with good rates of locoregional control and survival, comparable to those reported in the literature.*

Key words: breast neoplasms – surgery; survival analysis

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Introduction

Breast conserving therapy has been used since the 1960s and is now considered best practice in the treatment of early breast cancer. Retrospective and prospective randomized trials demonstrated that breast conserving therapy (BCT) produces rates of survival

and locoregional control similar to those of mastectomy.[1] Breast conserving surgery removes a detectable disease in the breast and/or regional lymph nodes, but has no effect on possible undetected disease in the remaining breast, chest wall, regional lymph nodes or distant sites.[2] By combining surgery, radiotherapy and adjuvant systemic therapy we can lower the risk of locoregional and distant recurrence.

In spite of this combined therapy there are still patients who develop recurrences. Local recurrence rates of 5-20% have been reported in different studies after BCT.[1-3] Although the impact of local recurrence on overall survival is not well established, it has a detrimental psychological effect on the patient.[1,4,5] By identifying those patients who have higher risk of developing a locoregional and/or distant recurrence, we can determine the right treatment to minimize the risk.[1]

The purpose of this retrospective study was twofold. First of all, to present a 5-year survival and locoregional control rates in patients treated at Institute of Oncology in Ljubljana and, secondly, to establish the eventual impact of treatment and patient characteristics on locoregional control and survival.

Methods

From January 1998 to December 1999 564 breast cancer patients stage I and II were treated at the Institute of Oncology Ljubljana with breast conserving therapy. The patient data were obtained by medical records. We evaluated the following patient and tumour characteristics: age, histological diagnosis, grade, size, number of metastatic lymph nodes, hormonal receptor status, extensive intraductal component (EIDC), vascular invasion, pathologic tumour margins, type of surgery and use of adjuvant therapy. We recorded eventual locoregional and/or distant recurrence by the retrospective analysis.

Statistical univariate analyses were done using the SPSS program. A statistical significance was assessed with Log-rank, Breslow and Tarone-Ware tests.

Results

Patient and tumour characteristics

The patient's age ranged from 28 to 77 years. The mean age was 54.2 years. The age distribution is presented on the histogram (Figure 1).

Most of the tumours were present in the upper outer quadrant (45%), followed by the outer lower quadrant (11%). Invasive ductal carcinoma (IDC) was by far the most common histological diagnosis (82.4% of tumours), followed by invasive lobular carcinoma (ILC) (10.6%) and ductal carcinoma in situ (DCIS) (2.6%). Other histological types of tumours were rare. The grade was more evenly distributed. The most common was Grade 2 with 44%, followed by Grade 3 with 33% and Grade 1 with close to 26%.

Most of the tumours were T1 (72%) and T2 (42%). Tis was present in 3% of cases. Sixty-six % of patients had negative axillary lymph nodes, 25.7% had one to three metastatic lymph nodes and 7.6% had more than three metastatic nodes.

Positive estrogen receptors were detected in 66.4% of tumours and positive proges-

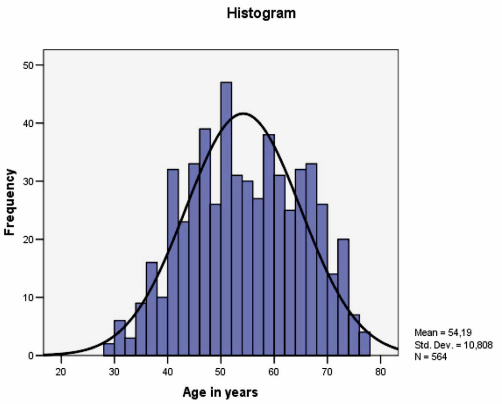

Figure 1. Age distribution of the patients.

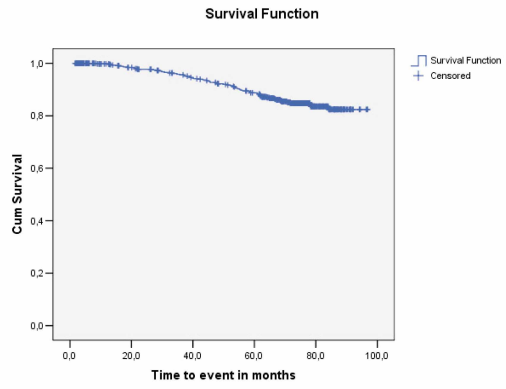

Figure 2. Overall survival of patients.

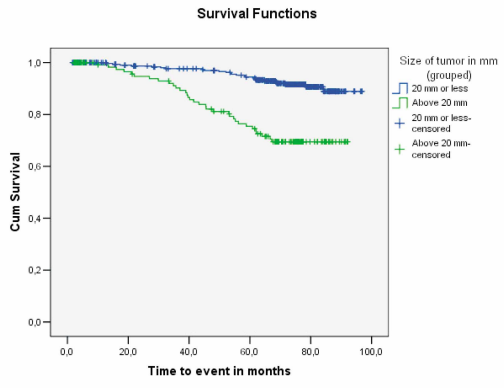

Figure 3. Impact of the tumour size on survival (p = 0.000).

terone receptors in 51.1%. Vascular invasion was present in 2.6% of tumours and 15% of tumours had an EIDC.

Treatment

All patients were treated with breast conserving operation, either tumorectomy or quadrantectomy. All patients received postoperative radiotherapy with two tangential fields. The total dose was 50 Gy followed by a boost with electrons to the tumour bed of 10 to 16 Gy. In patients with more than three metastatic axillary lymph nodes, 50 Gy was given to the supraclavicular fossa. No patient received radiotherapy to the axilla. About half of patients received adjuvant chemotherapy (54%) and hormonal therapy (50.4%).

Survival

The 5-year overall survival rate was 88.5% (Figure 2).

Prognostic factors for survival

In the context of our analysis, age and histology proved statistically non significant, while the influence of tumour size, nodes, grade, estrogen and progesterone receptors, vascular invasion and local and regional failure was significant.

As expected, a larger tumour leads to a lower survival probability (Figure 3). In this case as well as in other presented graphs, that will follow, the difference was statistically significant.

Comparing the overall survival rate (88.5%), in patients with Grade 3 tumours it was well below 80%, while for the patients with Grade 1 tumours it was close to 100% (Figure 4).

The patients who had tumours with positive estrogen and progesterone receptors had higher survival probability (Figures 5, 6).

The patients with a local recurrence had lower survival probability (Figure 7). The same holds for regional recurrence (Figure 8). For these patients the 5-year survival was just above 20%.

Vascular invasion proved to be a statistically significant prognostic factor. For patients with tumours with vascular invasion, the 5-year survival was just above 20%. We have to mention the problem of missing data for this particular prognostic factor, so we should be careful when interpreting the results.

Prognostic factors for local recurrence

The local recurrence occurred in 4.3 % of patients. Since the number of cases with local recurrence was small we used a simple cross-tabulation analysis (Table 1).

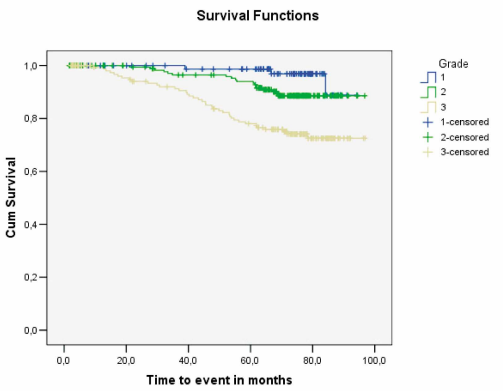

Figure 4. Impact of the tumour grade on survival (p = 0.000).

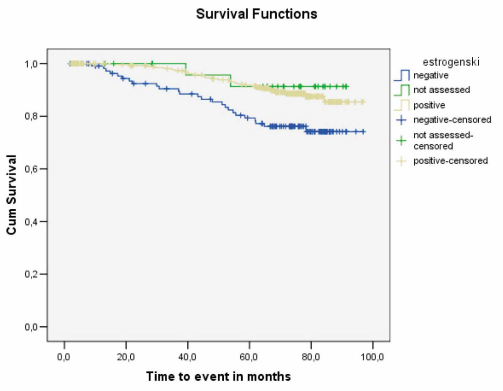

Figure 5. Impact of the tumour estrogen receptors on survival (p= 0,004).

Tumour grade, number of metastatic lymph nodes, surgical margins and hormonal receptors were prognostic factors for development of local recurrence.

Prognostic factors for regional recurrence

The regional recurrence occurred in 3.4% of patients. The total number of recurrences was 19. The total number of patients with metastatic axillary lymph nodes was 188. One recurrence was in the axilla, one in the parasternal region and 17 in the supraclavicular region (Table 2).

The small number of events is a problem for statistical analysis. However, the number of metastatic lymph nodes in the axilla is a risk factor for supraclavicular recurrence in our patients.

Discussion

In the study we tried to evaluate the 5-year survival and locoregional control in our patients after BCT and to establish eventual prognostic factors. The overall 5-year survival was 88.5%. This result is similar to other studies.[1] Prognostic factors that had an impact on the survival were tumour size, nodes, grade, estrogen and progesterone receptors, vascular invasion and local and regional failure.

As expected, larger tumours led to lower survival probability. There was a marked difference between tumours with diameter less than 2 cm compared to those with more than 2 cm (90% versus 70% 5-year survival).

There was also a marked difference regarding the tumour grade with lesser survival

Table 1. Prognostic factors for local recurrence

Prognostic factor	% of Local recurrence
Grade	Grade 1 – 1.8%
	Grade 2 – 3.6%
	Grade 3 – 7.8%
Number of metastatic axillary lymph nodes	0 – 2.7%
	<3 – 5.5%
	>3 – 14%
Margins	Free margins – 2.7%
	Involved – 12.5%
Estrogen, progesterone	Negative receptors → higher chance of local relapse

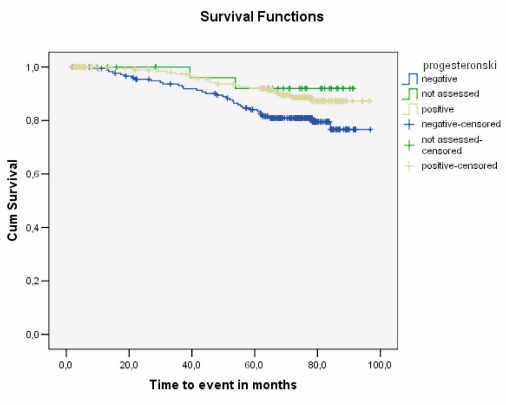

Figure 6. Impact of the tumour progesterone receptors on survival (p= 0.03).

probability in patients with less differentiated tumours.

The number of metastatic axillary lymph nodes is a well established prognostic factor[2] which was also confirmed in our study. Patients with negative lymph nodes had 90% 5-year survival probability, while those with more than three metastatic nodes had only 40%.

The presence or absence of hormone receptors had also an impact on the survival. Those patients who had positive receptors had higher survival probability. The same is true for patients who had tumours without vascular invasion. We have to mention that a lot of data was missing for this variable, so we can not be conclusive regarding this prognostic factor.

Table 2. Number of metastatic lymph nodes and percentage of regional recurrence

No of metastatic lymph nodes	% of regional recurrence
0	1.6
1-3	6.3
>3	9

Local and regional failure influenced the survival. A recent meta-analysis confirmed the impact of local recurrence after BCT on survival which is similar to the impact of a recurrence after modified radical mastectomy. It is estimated that for 4 local relapses avoided 1 life will be saved.[1,2,6]

Interestingly, age was not a significant prognostic factor for the survival.

The local recurrence occurred in 4.3% of patients. This is comparable to other studies, where the local failure ranges from 1.2-20%.[1,7-9]

We tried to identify the prognostic factors for local recurrence, but the small number of patients with local recurrences made the analysis difficult. We found some impact of grade (higher grade, more recurrences), number of metastatic lymph nodes (more metastatic lymph nodes, more relapses), surgical resection (patients with involved margins had

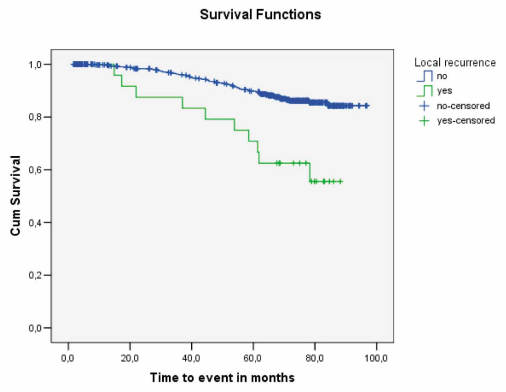

Figure 7. Impact of the tumour local recurrence on survival (p= 0,000).

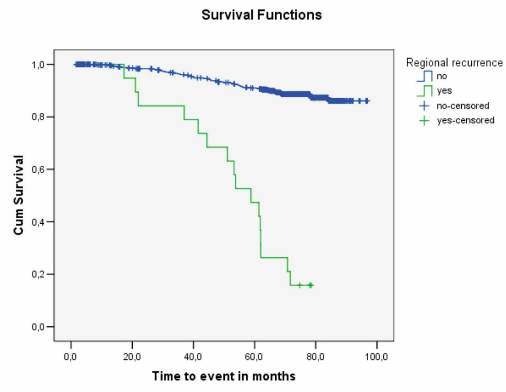

Figure 8. Impact of the tumour regional recurrence on survival (p= 0,000).

more local recurrences) and the receptor status (positive receptors, better prognosis).

The regional recurrence was less common, with 3.4% of patients. Most of the regional recurrences developed in the supraclavicular fossa and only one in the axilla.

Therefore we conclude that there is no need to irradiate the axilla after an axillary dissection even if metastatic lymph nodes were found at the operation.

Conclusions

Survival and locoregional control rates in our patients are comparable to those reported in the literature. Axillary recurrence is rare after an axillary dissection even in patients with >3 metastatic lymph nodes without RT to the axilla.

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