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The analysis of the outcome and the risk factors of failure in early breast cancer patients after breast conserving therapy

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Aim. To assess the outcome and to analyze the risk factors of failure and death in breast cancer patients treated with breast conserving therapy.
Material and method. 184 breast cancer patients in stage I and II were treated conservatively at the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, between 1995 and 1998. The time of observation was 48-84 months, median time – 70 months. In 53% of patients (98/184) adjuvant chemo- and/or hormonotherapy was introduced. The probability of local recurrence, disease free survival and overall survival were assessed using the Kaplan-Meier method. Risk factors of local/distant failures analyzed were analyzed with Cox's regression model and covered the following: age, hormonal status, familial breast cancer, laterality of the breast, medial versus other breast tumor location, non-palpable disease (lesions only in mammography) vs palpable, pathological stage pT and pN, number of excised or involved axillary nodes, histological type and grade of cancer, presence or lack of intraductal component and size of healthy tissue margin around the tumor.
Results. Recurrence (local recurrence or /and distant metastases) occurred in 9.8% of patients (18/184). Local recurrence was found in 5.5% of patients (10/184). The probability of 5-year disease free survival and 5-year overall survival was 91% and 97%. Based on multivariate analysis the only statistically significant risk factor of recurrence or death was palpable disease ($p<0.01$). The risk of failure was 6.7 fold higher in patients with palpable tumours, as compared to those with non palpable disease in the breast. The diameter of the tumor was, statistically, the most important risk factor of death ($p<0.01$). Patients with pT2 tumours had an 8.4 fold higher risk of death as compared to pT1 patients.
Conclusions. The results of breast conserving therapy performed in stages I and II of breast cancer (at the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology) are comparable to the published ones and demonstrate, that patients were adequately qualified and treated. The most important risk factor of failure and death was the size of the tumor. The best prognosis characterizes patients with pre-clinical breast cancer, where the primary tumor may be detected only mammographically and is less than 2 cm in diameter.

Analiza wyników i czynników ryzyka nawrotu u chorych na raka piersi po leczeniu oszczędzającym we wczesnym stopniu zaawansowania

Cel. Ocena wyników leczenia i analiza czynników ryzyka nawrotu i zgonu u chorych na raka piersi po leczeniu oszczędzającym.
Materiał i metoda. W Centrum Onkologii w Warszawie w latach 1995-1998 leczono w sposób oszczędzający 184 kobiety chore na raka piersi w I i II stopniu zaawansowania. Czas obserwacji wynosił 48-84 miesiące, mediana – 70 miesięcy. U 53% chorych (98/184) zastosowano uzupełniającą chemio- lub/i hormonoterapię. Prawdopodobieństwo przeżycia obliczano metodą Kaplana-Meiera. Wpływ potencjalnych czynników prognostycznych na czas przeżycia całkowitego i czas przeżycia bezobjawowego analizowano posługując się modelem proporcjonalnego ryzyka Cox'a. Do analizy włączono następujące czynniki: wiek, stan hormonalny, rodzinne występowanie raka piersi, strona piersi, lokalizacja raka w gruczole piersiowym przyśrodkowa versus inna, postać przedkliniczna (rak stwierdzany tylko w mammografii) vs postać kliniczna, stopień zaawansowania pT, pN, liczba usuniętych lub zajętych węzłów chłonnych, typ i stopień złośliwości histopatologicznej raka, obecność komponentu CDIS (raka przedinwazyjnego) w raku inwazyjnym i szerokość marginesów tkanek zdrowych wokół raka.

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Wyniki. Nawrót choroby (wznowa miejscowa lub/i przerzuty odległe) stwierdzono u 9,8% chorych (18/184). Wznowa miejscowa wystąpiła u 5,5% chorych (10/184). Prawdopodobieństwo 5-letniego przeżycia bezobjawowego i całkowitego wynosiło odpowiednio 91% i 97%. Na podstawie analizy wieloczynnikowej jedynym istotnym statystycznie czynnikiem, mającym związek z ryzykiem wystąpienia nawrotu lub zgonu, była postać kliniczna raka ($p<0,01$). Chore z klinicznie stwierdzanym rakiem miały 6,7 razy wyższe ryzyko nawrotu niż chore z rozpoznaniem przedklinicznej postaci raka. Na ryzyko zgonu istotny statystycznie wpływ miała wielkość guza ($p<0,01$). Chore z rozpoznaniem pT2 miały 8,4 razy wyższe ryzyko zgonu niż chore z pT1.

Wnioski. Wyniki oszczędzającego leczenia chorych na raka piersi w stopniu I i II, przeprowadzonego w Centrum Onkologii w Warszawie, są porównywalne z danymi z piśmiennictwa i świadczą o właściwym doborze chorych oraz o poprawnie przeprowadzonym leczeniu. Najważniejszym czynnikiem ryzyka nawrotu choroby lub zgonu po leczeniu oszczędzającym jest wielkość guza pierwotnego. Najlepsze rokowanie mają chore z przedkliniczną postacią raka (rak wykryty na podstawie mammografii) z guzem o średnicy do 2 cm.

Key words: breast cancer, conservative treatment
Słowa kluczowe: rak piersi, leczenie oszczędzające

Introduction

Breast conserving therapy provides an alternative to mastectomy in patients with early breast cancer. If the choice of patients is appropriate the late results of treatment are as good as in the case of mastectomy, while its supremacy lies in organ preservation [1, 2]. This is very important in view of the modern approach to cancer treatment, where quality of life is becoming an issue of increasing importance.

The first institution in Poland to introduce breast conserving therapy and to publish early results was the Clinic of Oncological Surgery of the Medical Academy in Łódź, where first such procedures were performed in 1981 [3, 4]. Over the next years many other oncological institutions adapted this method. Until today numerous papers concerning this issue have been published in Poland, devoted not only to the efficacy of breast conserving therapy, but also to the quality of life and to the aesthetic effect of this modality [3-11]. At the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw the protocol for breast conserving therapy had been prepared and introduced in 1984. One of its authors is now the co-author of this publication (MN). The method was widely introduced in 1995, after the establishment of the Department of Breast Cancer and since then it has been one of the main research fields at our institution [12]. Our previous papers have presented our experiences regarding treatment tolerance, complications and the psychological aspects of breast conserving therapy [6-8, 10, 11]. Basing upon the evaluation of 100 patients treated at our department between the years 1995 and 1997 after a follow-up period of 29 months the aesthetic effect was evaluatedh as excellent and very good in 88% of cases. However, concomitant chemotherapy and radiotherapy decreased the likelihood of achieving an excellent aesthetic effect. Similarly, a boost to the tumour site achieved through the implantation of Ir 192 provided a worse aesthetic effect than electron treatment; however this data must be carefully approached, as it originated from the time of our early experiences with breast brachytherapy [8]. We had concluded that treatment tolerance is good, but adjuvant radio-chemotherapy increases the duration of systemic treatment [6]. A majority of patients (87%) were satisfied with breast conserving treatment [10]. After three years of follow-up the main complication we had observed was oedema of the upper extremity induced by axillary lymphadenectomy. It was recognized in 10% of patients, however in a majority of them (88%) the difference in diameter between the two upper extremities did not exceed 2-4 cm [11].

The aim of the present paper is to summarise and evaluate the results of breast conserving therapy, including the ratio of local failures, time to recurrence and overall survival and to analyze the risk factors of treatment failure.

Material and method

Breast conserving therapy (BCT) is being performed at the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Onocology in Warsaw since 1995. Between January 1995 and December 1998 BCT was performed in 197 patients with breast cancer in stage 0, I and II. 184 patients stage I and II were fianlly included in this analysis, the remaining 13 patients had preinvasive breast cancer and will form the subject of a different analysis. Follow-up time was 48 to 84 months; median: 70 months.

Patient characteristics are presented in Table I. Mean age was 52 yrs; approx. 2/3 of the patients were pre-menopausal. Pre-clinical stage tumours (recognized in mammography only) were found in 72/184 pts (34%). The first stage of BCT consisted of lumpectomy (169/184 – 92%) or quadrantectomy (15/184 – 8%) and axillary lymphadenectomy of all three levels of lymph nodes. The median number of excised lymph nodes was 16. All patients were operated radically, with negative margins. If the lumpectomy margins were found to contain cancerous cells or the margin was less than 1 mm the patients were re-operated to achieve normal tissue margins (29 cases). Only in 5% of patients initially treated outside the MSCMCC the size of the margins was not evaluated pathologically in milimeters, although the samples were consulted and the procedure was pronounced as radical. All these patients had undergone quadrantectomy.

Tumours below 2 cm in diameter were found in 154/184 (83%) of patients; 2-3 cm in 17% of patients. In 141/184 (77%) of pts. the axillary lymph nodes we not affected (pN0), while in the remaining 43/184 (23%) of patients the axillary lymph nodes

Table I. Clinical characteristics of 184 patients

No. of patients	184 (100%)
Age (yrs) min 25. max 76, mean: 52	
25-45 yrs	62 (33)
46-55 yrs	63 (34)
56-75 yrs	62 (33)
Menopausal status	
Pre-menopausal	127 (69)
Post-menopausal	57 (31)
Familial breast cancer:	
No	164 (89)
Yes	20 (11)
Breast:	
Right	80 (43)
Left	104 (57)
Tumour localisation within the breast:	
Medial	63 (34)
Other	121 (66)
Cancer stage:	
Pre-clinical	72 (39)
Clinical	112 (61)
Advancement grade:	
I	150 (82)
II a	28 (15)
II b	6 (3)
pT1a + pT1b	65 (36)
pT1c	89 (48)
pT2	30 (16)
pN0	141 (77)
pN1	43 (23)
No. of excised nodes:	Min. 5, max. 34, mediana 16
No. of involved nodes:	
0	141 (77)
1-3	34 (18)
>3	9 (5)
Histopathological type of tumour:	
Carcinoma ductale	115 (63)
Carcinoma lobulare	36 (19)
Other types	33 (18)
Grade of histological malignancy	
G1	41 (22)
G2	53 (29)
G3	42 (23)
No evaluation	48 (26)
CDIS component in invasive cancer:	
Yes	50 (27)
No	134 (73)
Margins around tumour:	
1-2 mm	36 (19)
3-5 mm	47 (26)
>5 mm	91 (50)
No data	10 (5)
Treatment methods:	
BCS + RT	85 (46)
BCS + RT + CT	39 (21)
BCS + RT + HTH	45 (25)
BCS + RT + CT + HTH	15 (8)

BCS – Breast Conserving Therapy, RT – Radiotherapy, CT – Chemoterapy, HTH – hormonotherapy

contained metastases. After surgery the patients underwent irradaiation with a cobalt beam to the breast (102 pts) or with X photons 4MeV (82 pts) from 2 diagonal fields with the isocenter technique in 2 Gy conventional fractions to the total dose of 50 Gy over 5 weeks. Then we applied a boost to the tumour site (increased by 10 Gy) with an electron beam of individually assigned energy (113 pts) or with HDR brachytherapy (Ir 192) (71 pts). 3D treatment planning was performed with the aid of a simulator and CT scanning. The irradiated volume consisted of the breast, with CT planes every 2 cm. The irradiated areas were drawn into each plane. The method was consistent with ICRU 50 regulations (as described in an earlier paper) [13]. During treatment planning extra care was taken to shield the organs at risk (i.e. the heart and the lungs). Radiotherapy as the sole adjuvant modality or in conjunction with tamoxifen hormonotherpy was initiated 4-8 weeks after surgery. Post-operative chemo- and/or hormonotherapy was administered to 99 pts (54%). CMF chemotherapy (cyclophosphamide, methotrexate and 5-FU) was administered to 50 pts; epirubicine/CMF chemotherapy to 2 pts and AC chemotherapy (adriamycine, cyclophosphamide) to 2 pts. Tamoxifen hormonotherapy was administered to 60 pts, of which 15 received it after previous chemotherapy. Patients treated acc. to the CMF program were administered radiotherapy to the affected breast simultaneously with chemotherapy. Irradiation was initiated after the second course of CMF. Patients administered anthracyclines were treated sequentially, i.e. irradiation was applied after chemotherapy. In the case of 9 pts (5%) in whom metastases were present in more than 3 axilllary nodes radiation therapy was applied to the breast and to the regional lymph nodes. In these patients radiotherapy was also applied after the completion of chemotherapy.

We analyzed overall survival (OS) and disease free survival (DFS). The first confirmed recurrence of the malignancy was considered as failure (local failure and/or distant metastases or death). Survival probability was calculated acc. to the Kaplan-Meier method. The influence of potential prognostic factors on OS and DFS was analyzed acc. to Cox's proportional hazards model, which included the following prognostic factors: age, hormonal status of pts, familial breast cancer occurrence, the side of the disease, localization within the breast (paramedial vs. others), pre-clinical disease (recognized in mammography only) vs clinical stage, pT stage, pN, the number of excised and metastatic lymph nodes, type and grade of histopathological malignancy, presence of DCIS (a component of pre-invasive cancer) within invasive tumours and the healthy tissue margins around the tumour.

In the modeling process we applied a technique of stepwise elimination including (in course) the variable for which the critical test value (p) was the greatest, but not less than $p = 0.1$. Statistical significance level was set at 0.05.

Results

Recurrence was observed in 18/184 pts (9.8%) – in 10 cases local (5.5%) and in 8 – distant metastases (4.3%). Of the 10 pts with local failure in 7 the recurrence occurred in the tumour site, in 2 – outside the tumour site and in 1 case recurrence within the tumour site was accompanied by metastases to regional lymph nodes. The time to local recurrence varied between 14 to 72 months from the termination of primary treatment. Table II presents the characteristics of the 10 pts. with local failure, including the risk factors.

The time to distant metastases varied between 10 and 72 months. Death due to metastases occurred after 27-66 months.

Table II. Characteristics of 10 patients with local or locoregional recurrence

Factor	Ratio of patients with recurrence
Advancement:	
Grade I	6/150 – 4%
Grade II	4/34 – 11%
Stage:	
Pre-clinical	1/72 – 1.3%
Clinical	9/112 – 8%
Age:	
≤ 40 yrs of age	3/18 – 17%
> 40 yrs of age	7/179 – 4%
Healthy tissue margins:	
1-2 mm	2/36 – 5%
>2 mm	8/148 – 5%
CDIS component:	
Yes	7/50 – 14%
No	3/134 – 2%
Histological malignancy G:	
1 and 2	3/94 – 3%
3	7/42 – 16%
Nodal metastases:	
Yes	1/43 – 2%
No	9/141 – 6%
Adjuvant therapy (chemo-; hormono-)	
Yes	7/99 – 7%
No	3/85 – 4%

In 10/184 pts. (5.4%) we discerned a second malignancy: in 6/184 (3.2%) cancer of the ipsilateral breast, in the remaining cases ovarian cancer, endometrial cancer, lung cancer and meningioma.

5-year OS and DFS with a 95% confidence interval was 97% (95%, 99%) and 91% (88%, 94%), respectively (Figures 1 and 2). 5-year survival without local recurrence was 95%.

The results of the regression analysis are presented in Tables III and IV. In a multivariate analysis the only statistically significant factor ($p<0.01$) influencing the risk of recurrence (local failure and/or distant metastases)

Table III. Results of Cox's regression model analysis – risk of failure (local recurrence or/and distant metastases)

Variable	Beta factor	Standard deviation	Critical test level (p)	Relative risk (RR)
Clinical form	1.894	0.747	**0.01**	**6.7**

Table IV. Results of Cox's regression model

Variable	Beta factor	Standard deviation	Critical test level (p)	Relative risk (RR)
pT2 vs pT1	2.128	0.821	**0.01**	**8.4**
No. of excised nodes	0.113	0.056	**0.04**	**1.12**

or death was the clinical stage of the malignancy. Patients with clinically discernible cancers had a 6.7 times higher risk of recurrence or death than patients with pre-clinical tumours (discernible in mammography only). The risk of death was statistically significantly associated with the size of the breast tumour (pT) ($p<0.01$). In case of pT2 tumours the risk of death was 8.4 times higher than in the case of lesser tumours. We also discerned the significant influence of the number of excised lymph nodes on the risk of death ($p<0.04$). The relative risk was 1.12, i.e. a mean increase in the risk of death by 12% for each excised lymph node. DFS and OS survival for the most imminent prognostic factors listed above evaluated acc. to Cox's multivariate analysis is presented on Figures 3 and 4. Basing upon Cox's model of proportional hazards we have not discerned the influence of age, hormonal status, familial occurrence of breast cancer the side of the disease, localization within the breast (paramedial vs. others), pN, the type and grade of histopathological malignancy and presence of DCIS (a component of pre-invasive cancer) within invasive tumours on either OS and DFS.

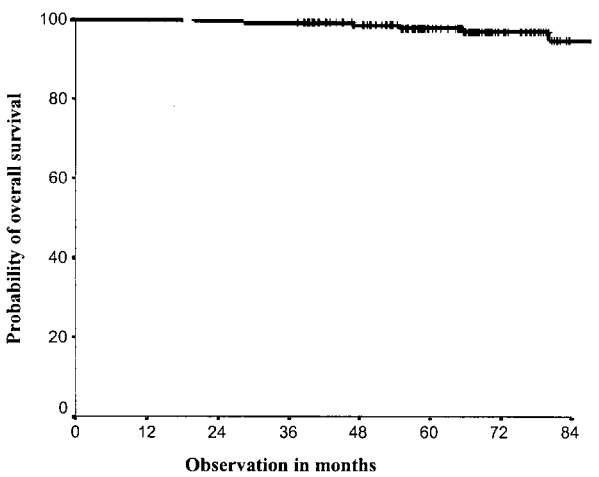

Figure 1. Overall survival of 184 patients with early breast cancer after breast conserving therapy

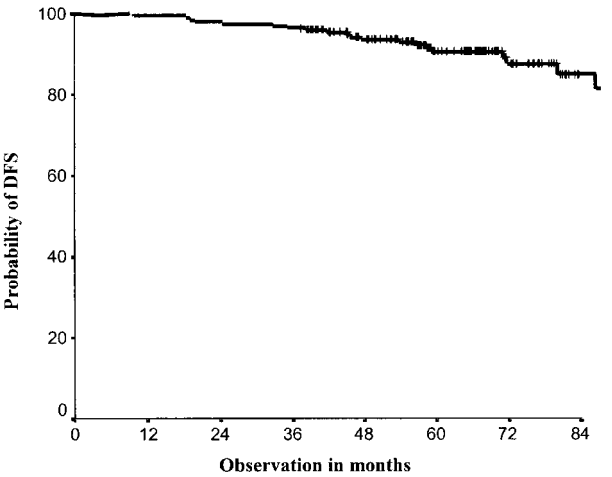

Figure 2. Disease-free survival of 184 early breast cancer patients after breast conserving therapy

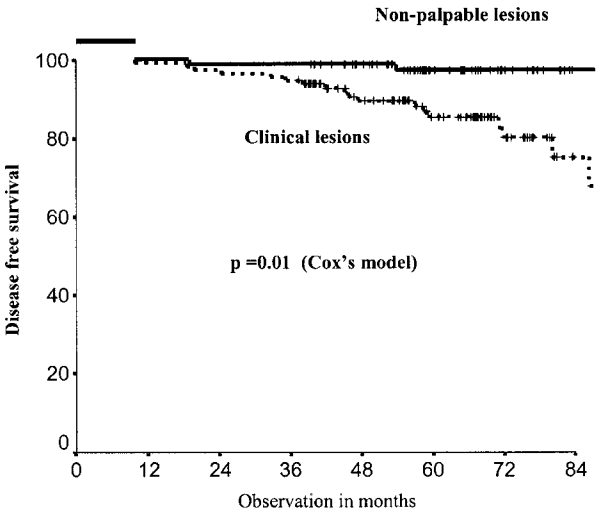

Figure 3. Disease-free survival of 184 early breast cancer patients after breast conserving therapy- preclinical versus clinical disease

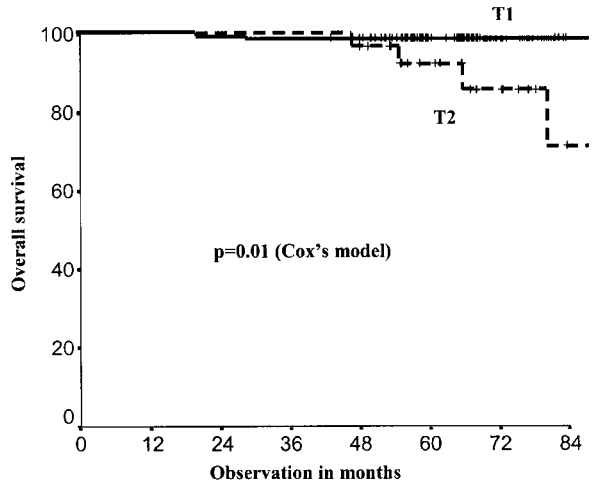

Figure 4. Overall survival in 184 early breast cancer patients after breast conserving therapy – pT1 versus pT2

Discussion

According to published data the risk of local failure in pts. with breast cancer after BCT (chemo- and radiotherapy) after 10 yrs of follow-up reaches 10-15% [2, 14-19]. Irradiation after BCT in advancement stage I and II reduces the risk of local failure by 30-40%, especially in patients with T2 tumours, infiltration of lymphatic vessels and axillary lymph node involvement [14]. Radiotherapy provides 6-9% of benefits for long-term OS, however in T1 pts with no nodal involvement the OS benefit is lower, not exceeding 5% [14].

Basing upon the results of prospective, randomized clinical trials it has been found that the risk of local failure after BCT and mastectomy is comparable [2, 15-19] and varies between 5% and 16%. In numerous retrospective studies the risk of local failure is 4-16% after 5-8 yrs; 10-21% after 10-12 yrs and 12-23% after 15 yrs [20-29].

In our material the ratio of local failures after 5 years of follow-up was 5.5%. This is similar to other published results and proves the adequate choice of patients at the onset of treatment and the correct course of surgery and adjuvant treatment.

In our patient material 5-year OS and DFS after BCT was 97% and 91%, respectively. This data is also consistent with that from literature, both Polish and international. Acc. to the results published by Jeziorski and Berner [3] 5-year OS and DFS was 97.8% and 93.4% respectively. Acc. to Jodkiewicz et al. [5] 5-year OS and DFS after BCT was 97% and 93%, respectively. In the study of Touboul et al. [25] performed on 528 women with breast cancer below 3 cm in diameter 5-year and 10-year OS after BCT was 93% and 86%, respectively, while DFS was 85% and 75%, respectively. In the study of Fredriksson [30], who had performed an analysis of 6613 pts who had undergone BCT the 5-year and the 10-year cancer associated survival was 84.5% and 70.9%, respectively. In other, less recent studies, 5-year survival after BCT varied between 50% and 84% [22, 31, 32].

Risk factors of local failure and distant metastases

Literature reports list a number of risk factors affecting local failure and distant metastases after BCT. Some are more characteristic for local failure, while others more typical for dissemination. There also exist some predictive factors for both these clinical situations.

Among factors listed as affecting local failure after BCT one finds young age, large tumour mass, multifocal carcinoma, high degree of histological malignancy, high component of DCIS and the size of the healthy tissue margin around the tumour. The most common risk factors of dissemination after BCT include age below 35 yrs, the size of the primary tumour, axillary lymph node involvement, high grade of histopathological malignancy, invasion of cancer cells into vessels, lack of estrogen and progesterone receptors within the cancer cells and local failure [14, 25, 26, 28].

In our study we have not analyzed vessel infiltration and the presence of estrogen receptors, because they were only evaluated in approx. half of the patients.

Patient age

The most important risk factor of local failure, confirmed in numerous retrospective studies and in large randomized trials is patient age. In women below 35 yrs. of age the risk of local failure after BCT reaches some 24%-43% after 8-10 yrs. of follow-up [20-25, 33-37]. It remains high in the 35-40 yr. age group [26, 29, 38, 39]. Voogd et al. [34] have shown an over 9-fold increase in the risk of local recurrence in women below 35 yrs of age, as compared to women over 60 yrs of age. Arriagada [37] reports a higher local failure ratio in women before 40 yrs. of age. In a randomized EORTC clinical trial performed by Bartelink et al. [40] it has also been shown that the recurrence risk was significantly dependant on patient age. Patients below 40 yrs. of age had the greatest risk

of recurrence and were the ones to benefit the most from a boost to the tumour site (19.5% of recurrences in the first 5 yrs in the "no-boost" group, as compared to 10.2% after a 16 Gy boost). Young age is considered a risk factor of not only local recurrence, but also of developing distant metastases [41].

We divided our patient material into 3 age groups and evaluated the recurrence risk separately in each of these groups. We failed to show that age was a risk factor of recurrence or death. One of the reasons for such a result could be the relatively low ratio of treatment failures. At the same time in Table III we have shown that patients below 40 yrs. of age are at a greater risk of developing local recurrence, as compared to older women, which is similar to other literature reports.

Histopathological characteristics of the tumour

The local failure risk is higher in the case of multifocal tumours and reaches some 36-40% [25, 35, 36, 38, 42]. In the study of Touboul [25] it has been shown that microscopically bi-focal tumours up to 1 cm in diameter at a distance of less than 1 cm from one another pose as a risk factor of local failure despite healthy tissue margins of at least 2 mm. Vessel involvement around the primary tumour increases the risk of recurrence and dissemination [25, 35, 36, 42, 43].

A number of studies have shown that the presence of invasive or pre-invasive cancer cells within the healthy tissue margins surrounding the tumour increases the risk of local recurrence 2-3 times during a 10-year follow-up period [23, 29, 36, 42, 44-46]. After 5 years of follow-up local recurrence in patients in whom cancer cells were found in the healthy tissue margin reached 2-22.5%, while with free healthy tissue margins – 2-7% [18, 47]. In the course of the study of Park et al. [44] performed on 533 patients it has been shown that after 8 years of follow-up the local failure risk in patients with large and close margins was 7%, while in patients with the presence of cancer cells within the margins – 27%. Such correlations cannot be found in the course of studies where margins were routinely increased or where the boost to the tumour site was increased to 20-25 Gy [25].

The presence of extensive EIC components increases the risk of local failure [25, 34-36, 39, 48-50]. The reason behind this is probably the fact that in cases of large residue component of CDIS within the tumour margins it may be difficult to discern residual disease, even in places relatively distant from the primary tumour [48]. EIC is a typical risk factor of local recurrence, but not of distant metastases [14, 25, 34].

Among the different histological types of breast cancer only lobular carcinoma, especially multifocal, poses the greatest risk of local failure [39, 51, 52]. The high grade of histological malignancy may increase the risk of local failure, however not all authors support this theory [25].

At our institution we have introduced a system of qualification of patients for BCT as early as in 1995. Patients with multifocal tumours were not qualified for BCT, therefore we cannot perform an analysis of this particular risk factor. All patients were radically operated, achieving negative margins. We have performed a statistical analysis of the size of the healthy tissue margin (1-2 mm; up to 5 mm and over 5 mm) on the risk of recurrence, but arrived at no conclusive results. In our study group we did not observe an increased risk of recurrence related to the presence of the pre-invasive cancer component. Neither did we observe any relations between the risk of recurrence and the histopathological type of tumour. It may arise from the fact that lobular carcinoma, which poses the greatest risk of recurrence, was significantly less common in our patient material. Recurrence analysis has shown, that 9 out of 10 recurrences were related to ductal carcinoma, and only one out of ten to lobular carcinoma. To summarise, in the course of our study we have failed to find any statistically significant correlations between the histological type of tumour and the risk of local, locoregional or distant failure. This probably arises from the strictly followed protocol which sets exact criteria for patient qualification and forces the necessity of increasing healthy tissue margins.

TNM stage

Numerous authors have stressed the higher ratio of failures in patients with tumours greater than 1.5 cm [24], and especially in tumours greater than 2 cm, as compared to patients with smaller cancers [17, 18, 26, 29, 42, 43, 49, 53]. Also, there exist reports concerning the correlation between axillary lymph node involvement and the ratio of distant metastases [24].

In our material we have found that the stage of clinical advancement was the main cause of recurrence. Only patients with tumours of less than 3 cm were qualified for BCT, but the statistical analysis was performed basing upon the histopathological results concerning the pT characteristic. The risk of recurrence for clinically evident tumours was 6.7 times greater than in the case of pre-clinical tumours (i.e. discerned only in mammography). We have also found that in case of pT2 tumours the risk of death was 8.4 times higher than in the case of lesser tumours. Similar results have been reported in literature. In our material we have not confirmed the influence of axillary lymph node involvemenmt on prognosis. However, the number of patients with axillary lymph node involvement is very low in our material. On the other hand we did find that the risk of death increases statistically significantly ($p<0.04$) with the increase in the number of resected axillary nodes. The interpretation of this result is complex and demands further studies. In order to arrive at an explanation for such a phenomenon we have investigated whether there exists some form of relation between the number of excised nodes and the stage of cancer advancement. We assumed that in patients with more advanced disease the

surgeon removes a greater number of lymph nodes. Statistical analysis has shown that there exists no correlation between the number of resected lymph nodes and the TNM stage, the tumour size and the number of nodal metastases found during the histopathological examination (chi-square test: p=0.389, p=0.96 and p=0.49, respectively).

Adjuvant therapy

Systemic adjuvant treatment decreases the risk of local failure and of distant metastases [24, 38, 41, 44, 54-56]. Tamoxifen hormonotherapy [55] not only reduces the risk of recurrence, but also reduces the risk of cancer of the ipsilateral breast. In the study published by Mirza [24] patients on tamoxifen hormonotherapy had a 66% lower risk of local recurrence, as compared to patients not receiving hormonotherapy. Freedman et al. [57] have shown that adjuvant tamoxifen treatment in patients over 55 years of age was the most important factor reducing the risk of local recurrence. In patients between 36 and 55 years of age with ER and PR positive cancers the recurrence risk was 5% in those taking tamoxifen, and 20% in pts who were not on tamoxifene. Elkhuizen et al. [38] have concluded that chemotherapy reduces the local recurrence risk by 50% in patients below 43 yrs of age. Bucholtz et al [54] had observed 484 pts. with breast cancer without axillary lymph node involvement and found that systemically treated patients (chemotherapy, chemotherapy and tamoxifen or tamoxifen) have a 10% better local control after 8 years of follow-up. Thus it has been confirmed that tamoxifen as a sole modality, and chemotherapy also, provide benefits for local recurrence-free survival. According to the research team from the Dana Faber Hospital the delay in radiotherapy caused by sequential treatment consisting of chemotherapy followed by radiotherapy increases the risk of local failure [59], but Froud et al. [59] have not shown any differences in the ratio of local recurrence among low risk patients (in an entire group of 1962 patients) who began radiotherapy during a period of 20 weeks after surgery in the course of BCT and did not receive cytostatics over this time period. A majority of our patients who had received cytostatics (45/54 – 83%) were undergoing concomitant chemo-radiotherapy, which could have also had an impact on the good treatment results.

The analysis of our patient material has shown that in the case of breast cancer patients there exists a strong correlation between the size of the tumour (pre-clinical vs clinical and pT1 vs pT2) and the frequency of treatment failures (Figures 3, 4). These results are fully supported by data from literature. It appears that the relatively low risk of local failures and distant metastases arises from the correct choice of patients during initial qualification (early stages of disease, no cases of multifocal carcinoma) and adequately performed surgery (wide healthy tissue margins around the excised tumour) and adjuvant therapy.

Conclusions

1. The results of BCT in patients with breast cancer stage I and II treated at the Maria Sklodowska-Curie Memorial Cancer Cnter and Institute of Oncology in Warsaw are similar to those reported by other institutions and provide proof of appropriate patient qualification and treatment performance.
2. The most important risk factor of recurrence or death after BCT is the size of the primary tumour. Patients with pre-clinical tumours (discerned in mammography only) below 2 cm in diameter have the best prognosis.

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