

Full-thickness chest wall resection for locally recurrent breast cancer

Die allschichtige Thoraxwandresektion bei Lokalrezidiven des Mammakarzinoms

Abstract

Aim: In spite of available recommendations, therapeutic procedures of locally recurrent breast cancer are very different. In a retrospective study, the possibilities and results of complete, full-thickness chest wall resection are presented.

Methods: Between 1985 and 2004, 51 women underwent complete, full-thickness chest wall resection with primary coverage. Primary surgical therapy of breast cancer had been mastectomy in 88%. Median age of patients undergoing surgery for a local recurrence was 57 (29 - 81) years. The median interval between surgery of the primary tumour and of the local recurrence was 70.3 (10.7 - 327.2) months; median follow-up was 29.4 (1.8 - 230.9) months. 40 (78.4%) patients required rib resections, 15 (29.4%) of them in combination with partial sternal resection. In 4 (7.8%) patients complete and in 7 (13.7%) patients partial sternal resection without additional rib resection were performed. Coverage was mainly realized using latissimus dorsi myocutaneous flaps (n=44; 86.3%). Survival rates were calculated by means of the Kaplan-Meier method, the relative risk using univariate and multivariate Cox-regression analysis.

Results: In the total collective, cumulative 5-, 10- and 15-year survival (YS) rates were 39%, 31% and 23%, respectively, median survival 46.4 months. R0 resection was associated with a 5-YS of 42%. Prognostic factors were age at the time of primary surgery, disease-free interval and tumour invasion of bony structures. Mortality was 2%, morbidity 35%.

Conclusion: Full-thickness chest wall resection of locally recurrent breast cancer is possible in almost any patient when performed by a team of thoracic and plastic surgeons. Only radical resection provides good long-term results with low mortality and morbidity.

Keywords: chest wall resection, breast cancer, local recurrence, compartment resection, thoracic surgery, plastic surgery

Zusammenfassung

Vorhaben: Die Therapie des Lokalrezidives des Mammakarzinoms wird trotz vorliegender Empfehlungen sehr uneinheitlich durchgeführt. Mit der retrospektiven Untersuchung sollen die Möglichkeiten und Ergebnisse der kompletten, allschichtigen Brustwandresektion aufgezeigt werden.

Methode: Zwischen 1985 und 2004 wurde bei 51 Frauen eine komplette, allschichtige Thoraxwandresektion mit primärer Deckung durchgeführt. Die primäre, operative Therapie des Mammakarzinoms bestand bei 88% in einer Mastektomie. Das Alter betrug bei der Operation des Lokalrezidives im Median 57 (29 - 81) Jahre. Das mediane Intervall zwischen Primärtumoroperation und Lokalrezidivoperation betrug 70,3 (10,7 - 327,2) Monate, die mediane Follow-up Zeit betrug 29,4 (1,8 - 230,9) Monate. Rippen wurden bei 40 (78,4%) Patienten reseziert, bei

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15 (29,4%) in Kombination mit einer Sternumresektion. Bei 4 (7,8%) Patientinnen wurde eine komplette und bei 7 (13,7%) eine partielle Sternumresektion ohne zusätzliche Rippenresektion durchgeführt. Die Deckung wurde hauptsächlich mittels muskulokutaner Latissimus dorsi Lappen durchgeführt (86,3%, n=44). Die Überlebensdaten wurden mit der Kaplan-Meier Methode, das relative Risiko mit der univariaten und multivariaten Cox-Regression berechnet.

Ergebnisse: Die kumulative 5, 10 und 15-Jahresüberlebenszeit (Jü) beträgt für die gesamte Gruppe 39%, 31% und 23%, das mediane Überleben 46,4 Monate. Bei R0 Resektion beträgt die 5-Jü 42%. Prognostische Faktoren waren das Alter der Patientinnen bei der Primäroperation, das krankheitsfreie Intervall und die Tumordinfiltration von knöchernen Strukturen. Die Letalität betrug 2%, die Morbidität 35%.

Schlussfolgerung: Die allschichtige Brustwandresektion des Lokalrezidives des Mammakarzinoms ist im Team von Thorax- und plastischen Chirurgen nahezu immer möglich. Nur durch die radikale Resektion lassen sich gute Langzeiterfolge bei geringer Letalität und Morbidität erzielen.

Introduction

The locoregional recurrence of breast cancer is defined as the recurrence of a tumour in a previously operated or irradiated area of treated breast cancer. The incidence of local recurrences after mastectomy and breast-conserving therapy varies between 5% and 40% depending on risk factors and primary therapy [1]. So far, a standard therapy of local recurrences has not been defined. It is recommended to excise the visible tumour with subsequent radiation therapy. In many cases, however, irradiation or chemotherapy is performed primarily. Surgical therapy of local recurrences or chest wall metastases of breast cancer is either not performed at all or with an insufficient safety margin. Local recurrence is often misinterpreted as the first indication of a systemic dissemination of the disease and curative approach is therefore abandoned [2]. Still today large ulcerated chest wall tumours are seen. Whether radical resection of local recurrence offers palliative or curative approach or major prolongation of survival is still unclear. Moreover, chest wall resection is often regarded as a mutilating intervention with high morbidity and mortality. The possibility of chest wall resection with plastic coverage for complete resection of chest wall recurrences is almost unknown. Given a palliative approach, full-thickness chest wall resection provides a markedly improved quality of life and given a curative approach, a good chance for long-term survival. There are, however, very few reports on results of full-thickness complete chest wall resections for locally recurrent breast cancer with sufficient safety margins.

Patients and methods

Between 1985 and 2004, 51 women underwent complete, full-thickness chest resection with primary coverage. The term "local recurrence" was defined as a relapse of tumour manifestations after breast-conserving procedure in mammary region (primary surgical region), after radical

therapy in chest wall region, covering skin, scar tissue and remaining glandular tissue. Regional recurrence also includes the involvement of ipsilateral lymph nodes. We included only patients with local recurrences who met this definition.

Patient data were obtained retrospectively from the medical records. The present condition of the patients was documented either by regular outpatient follow-up or by obtaining information from the family physician, the patient herself or from relatives. Descriptive data on primary tumour treatment are listed in Table 1. 45 (88.2%) patients had primary breast resection, 6 (11.8%) breast conserving surgery. Tumour stages 1 and 2 were present in 76.5% of the patients, while it was unknown in 5 (9.8%) patients. The primary hormone-receptor status was unknown in 43.1% (n=22). 17 (33.3%) patients were known to have an adjuvant therapy.

Resection was performed according to following standards: The visible tumour was resected with safety margin of at least 2 cm, if possible 5 cm. If tumour invasion of a rib was suspected, cranial and caudal ribs were resected as well. In case of doubt of extension of tumour, frozen sections of the margins were performed.

At the time of surgical intervention of the local recurrence, median age was 57 (range 29-81) years. Disease free interval (DFI) was 70.3 months (M) (range 10.7-327.2 M). Median follow-up was 29.4 months (range 1.8-230.9 M), median follow-up of survivors 36.7 M (range 1.8-230.9 M). Except of 5 patients, in whom replacement of chest wall soft tissue was not necessary, all interventions were performed by a team of one thoracic and one plastic surgeon. Surgical data are detailed in Table 2. A mean of 3.2 (range 1-5) ribs were resected in 40 (78.4%) patients, in 15 (29.4%) of them in combination with a sternal resection. In 4 (7.8%) patients complete sternal resection and in 7 (13.7%) patients partial sternal resection without additional rib resection were performed. Median size of resected material was 100 (range 36-360) cm². Chest wall stability was restored mainly by non-absorbable polypropylene mesh (n=23, 45.1%) or by absorbable

Table 1: Characteristics of the primary breast cancer and treatment

	No. of patients
Age	
≤ 45 years	21
> 45 years	30
Hormonal status	
ER+/PR+	16
ER-/PR-	9
ER+/PR-	4
Unknown	22
Breast resection	
Modified radical mastectomy	44
Radical mastectomy	1
Breast conserving resection	6
Stage	
1	16
2a	14
2b	9
3a	5
3b	2
Unknown	5
Adjuvant treatment	
Radiation therapy	4
Chemotherapy	4
Radiation and chemotherapy (sequential)	4
Chemoradiotherapy (concurrent)	2
Hormonal therapy	1
Chemo- and hormonal therapy	1
Radiation and hormonal therapy	1
No therapy or unknown	34

polygalactin mesh (n=14, 27.5%), rarely (n=12, 23.5%) by Gore-tex. In two cases (3.9%), no patch was used. Coverage was mainly realized using a latissimus dorsi myocutaneous flap (n=44, 86.3%), in one case (2%) by a rectus abdominis myocutaneous flap, and in two cases (3.9%) a pectoralis major myocutaneous flap. No additional flap coverage was necessary in four cases (7.8%).

Survival was calculated using the Kaplan-Meier method, the impact on survival was determined for the different factors univariate by means of the log-rank test. Calculation was started at the time of chest wall resection and included postoperative fatalities. Relative risk and multivariate analyses were calculated by Cox Regression analysis. Proportional hazards as well as possible collinearities and interdependencies were considered.

The following factors were included: bone infiltration (yes-no); disease free interval (≤2 years - >2 years); metastases (yes - no); multilocular chest wall recurrence (yes - no); tumor diameter (≤3 cm - >3 cm); age at primary resection (≤45 years - >45 years).

Statistical analyses were computed using SAS (Vers. 8; SAS Institute, Cary, USA); Kaplan-Meier analyses and plots were performed using SPSS (Vers. 12; Chicago, USA).

Results

All patients were in good general condition (WHO grade IV). In all cases, the local recurrence was completely resected. Because of R1 resection one patient had to un-

dergo a second sternal resection after 10 days. Palliative R2 resection because of pleural carcinosis or dissemination of pulmonary metastases was performed in 6 patients. The diameter of resected tumour was 1-11 cm, median 3 cm, in case of multilocular tumour the largest diameter was considered.

Hospital mortality was 2%, i.e. one patient died postoperatively from pulmonary complications. Complications were observed in 33% (n=17). Bleedings needing revision were found in 14% (n=7), flap necroses in 3.9% (n=2), and wound infections in 7.8% (n=4), myocardial and respiratory insufficiency, recurrent nerve palsy and empyema in one patient respectively.

At the time of follow-up, 24 patients (47.1%) were still alive, 21 (87.5%) of them without any recurrence. Cumulative 5-year survival (5-YS) for the total collective was 41.1%, 10-year survival (10-YS) 28.5%, and 15-year survival 21.3%, median survival (MS) was 50.1 months.

Comparing patients with R0 resection to those with R2 resections, according to the above mentioned definition, 5- and 10-YS of completely resected patients (n=45) amount to 41.4 and 36.8%, respectively, with a MS of 46.7 months in contrast to a 5- and 10-YS in patients with R2 resections (n=6) of 41.7 and 0% with a MS of 57.2 months (p=0.33).

The following subgroup analyses of apparently prognostically relevant parameters included only R0 resected patients.

If the recurrence did not invade bony structures (n=28), 5- and 10-YS were 52.6% with a MS of 154.6 months. If there was a histologically proven bone invasion (n=17),

Table 2: Characteristics of the locally recurrent breast cancer and treatment

	No. of patients
Hormonal status	
ER+/PR+	16
ER-/PR-	18
ER+/PR-	6
ER-/PR+	3
Unknown	8
Chest wall resection	
Ribs only	25
Sternum complete	4
Sternum partial	7
Sternum and ribs	15
Number of ribs resected	
1	3
2	3
3	20
4	10
5	4
Unknown	3
Additional resection of	
Lung	9
Diaphragm	1
Pericard	3
Clavicula	2
Forequarter amputation	1
Reconstruction	
Polypropylen	23
Polygalctin	14
Goretex	12
None (no reconstruction required)	2
Skin closure	
Latissimus flap	44
Rectus flap	1
Rotation flap	2
None (no reconstruction required)	4
Radicality	
R0	45
R2	6
Previous treatment	
Resection 1 time	6
2 times	5
3 times	5
4 times	1
6 times	1
Radiotherapy	14
Chemotherapy with hyperthermia	1

5-YS was 19.8% and 10-YS 9.9% with a MS of 29.4 months ($p=0.03$) (Figure 1).

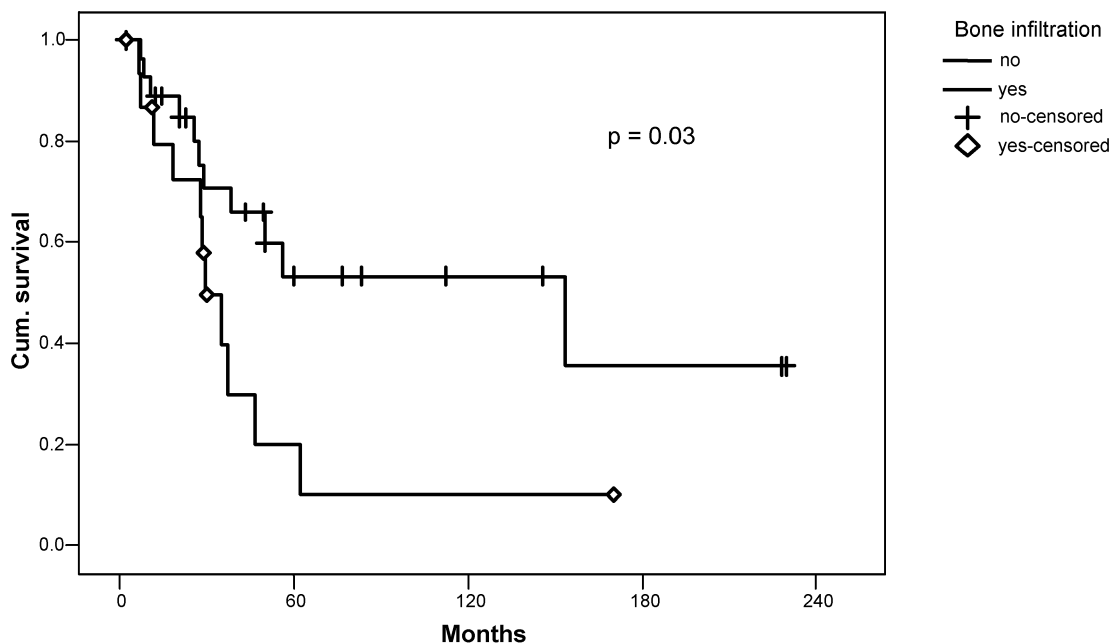
If additional metastases of lung, pericardium or diaphragm were resected ($n=9$), 5- and 10-YS were 19.4% with a median MS of 37.3 months. The group without metastases ($n=36$) had a 5- and 10-YS of 47.3% and 41.4%, respectively, with a MS of 56.6 months ($p=0.30$). If tumour size increases above 3 cm, survival apparently tends to deteriorate. A tumour size below 3 cm ($n=23$) was associated with a 5-YS of 49.3%, above 3 cm ($n=22$) with only 34.2% with a MS of 46.7 and 37.3 months, respectively ($p=0.43$).

With an DFI equal or more than 24 months ($n=38$), 5- and 10-YS are 47.8% and 41.8% with a MS of 56.6 months compared to a 14.3% 5- and 10-YS with a MS of

27.7 months if DFI was less than 24 months ($n=7$) (Figure 2) ($p=0.04$).

Another important factor is patient age at the time of primary surgery. Patients below 45 years of age at the time of primary therapy of breast cancer ($n=18$) had a better prognosis with a 5-YS of 70.5% and a 10-YS of 58.8%, with the median survival not being achieved so far. In contrast, women above 45 years of age at the time of primary therapy ($n=27$) had a 5- and 10-YS of 23.4%, with a MS of 29.4 months ($p=0.005$) (Figure 3).

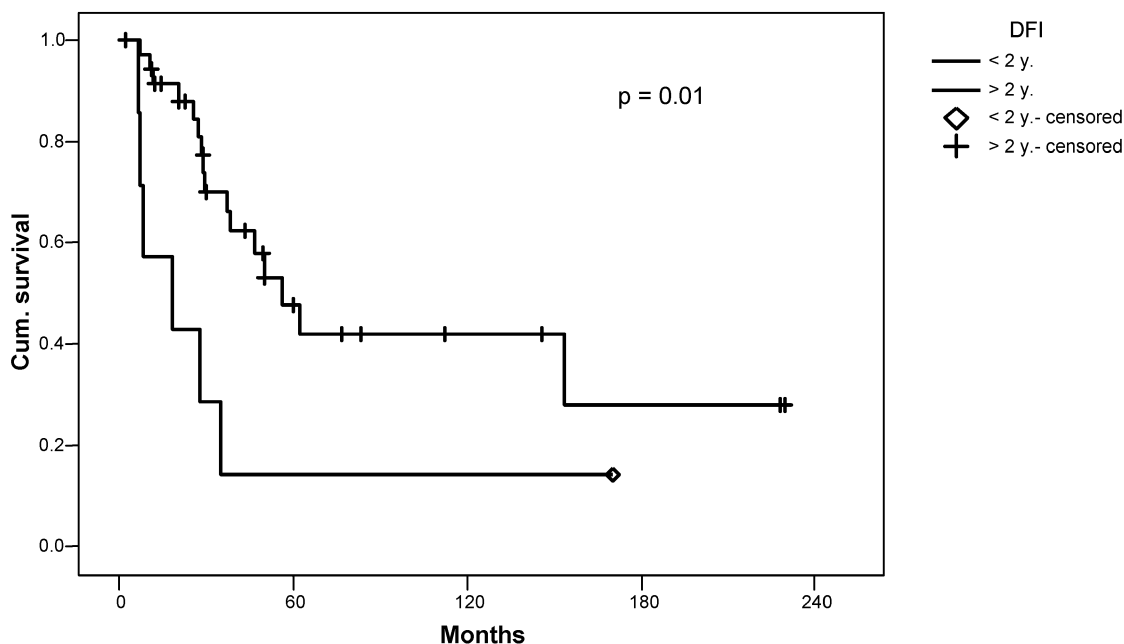
Comparing the p-values of survival probabilities calculated by Cox-Regression, there are demonstrative results for the expected prognostic factors bone invasion and disease-free interval with p-values < 0.05 . Additional metastases, multilocal manifestation of the recurrence and



Patients at risk

no	28	7	4	2	0
yes	17	2	1	0	0

Figure 1: Cumulative survival of complete resected (R0) patients by presence of bone infiltration



Patients at risk

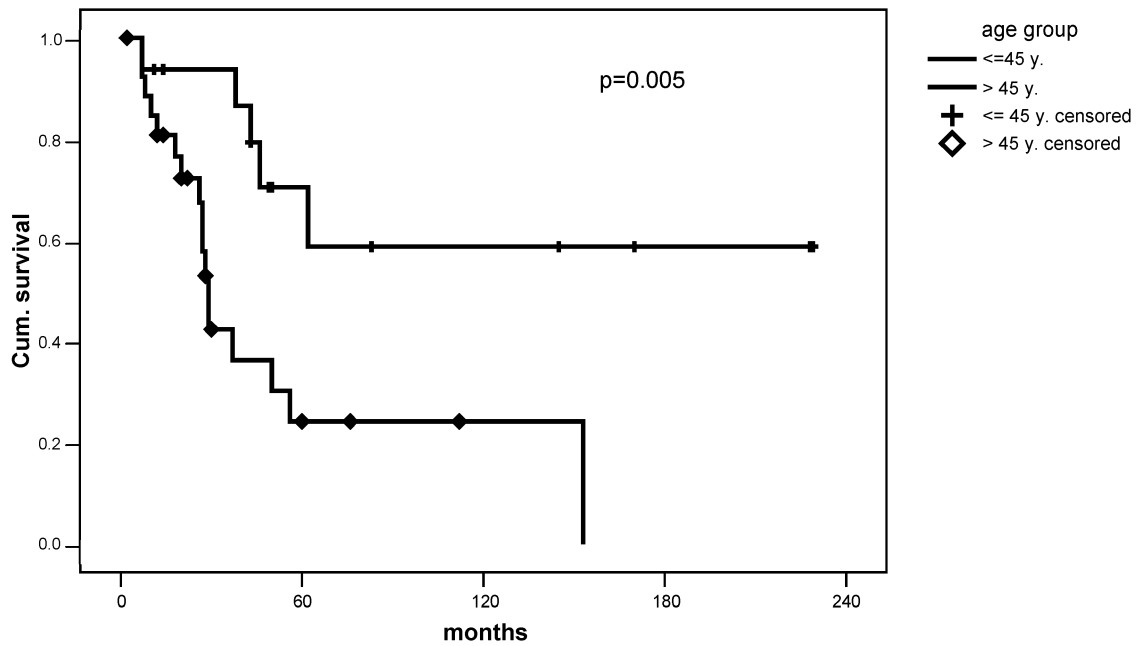
< 2 y.	7	1	0	0	0
> 2 y.	38	8	4	2	0

Figure 2: Cumulative survival of complete resected (R0) patients according to disease free interval

largest tumour diameter do not have impact on prognosis. Descriptive data are given in Table 3.

Risk ratio of univariate Cox analysis shows that patients with bone invasion had a 2.5 fold higher risk of premature death, patients with a disease-free interval of ≤ 2 years had a 3-fold increased risk and patients with additional metastases still a 1.6-fold increased risk. Patients above

45 years of age at the time of primary therapy had a 3.9-fold increased of risk of death. For tumour diameter and multilobar recurrence the best estimator of risk ratio is 1.5 and 2.3 respectively. Since the relevant confidence intervals are very broad, these data only indicate a trend, which however might become significant given a higher number of cases (Table 4).



Patients at risk					
< 45 y.	18	6	4	2	0
> 45 y.	27	3	1	0	0

Figure 3: Cumulative survival of complete resected (R0) patients according to age groups at the time of primary therapy

Table 3: Characteristics of prognostic factors

	all	R0
Bone infiltration		
yes	23 (45%)	17 (38%)
no	28 (55%)	28 (62%)
Multilocular recurrence		
yes	8 (16%)	5 (11%)
no	43 (84%)	40 (89%)
Metastases		
yes	14 (27%)	9 (20%)
no	37 (73%)	36 (80%)
Disease free interval		
≤ 2 years	7 (14%)	7 (16%)
> 2 years	44 (86%)	38 (84%)
Age groups at the time of primary operation		
< 45 years	21 (41%)	18 (40%)
> 45 years	30 (59%)	27 (60%)
Tumor diameter cm (median, range)	3 (1-11)	3 (1-10)
Resectat in cm ² (median, range)	100 (36-360)	100 (36-360)

Table 4: Univariate statistics of prognostic factors (patients with complete resection)

Factor	p	Risk-Ratio (95% Confidence Intervall)
Age cohort (<45>)	0.005	3.9 (1.4 – 10.7)
Bone infiltration	0.02	2.6 (1.1 – 6.1)
Disease free interval (DFI)	0.03	3.0 (1.2 – 7.4)
Metastases	0.30	1.6 (0.6 – 4.2)
Multilocular recurrence	0.38	0.5 (0.1 – 2.3)
Tumor diameter	0.35	1.5 (0.6 – 3.5)

Table 5: Multivariate statistics of prognostic factors (patients with complete resection)

Factor	p	Risk-ratio (95% Confidence interval)
Age at the time of primary therapy	0.002	6.1 (1.9 – 19.0)
Bone infiltration	0.04	2.8 (1.0 – 7.3)
Disease free interval (DFI)	0.08	2.6 (0.9 – 7.6)

The factors DFI, bone invasion and age at the time of primary therapy were analysed using multivariate Cox analysis, additionally. Only bone invasion and age at the time of primary therapy showed demonstrative p values below 0.05 and a risk of premature death which is 2.8 and 6.1 fold higher for patients with bone invasion and age > 45 years at the time of primary treatment respectively. The best estimator for the risk ratio of DFI was 2.6 (Table 5).

Discussion

A review of the literature showed that a complete chest wall resection is only performed in very rare cases. The largest collective reported on in the last 20 years includes 69 patients [3]. In our opinion, there are major therapeutic shortcomings in this field. Unfortunately, many patients are only referred for complete chest wall resection after multiple previous therapeutic procedures, not few patients came on their own initiative. In our group, 27 patients received a mean of 2.1 therapeutic procedures before final resection. One patient each had undergone 5 and 6 surgical interventions previously. 24 patients (47%) were primarily presented at our institution.

Guidelines on therapy of locally recurrent breast cancer do not provide a clear therapeutic strategy. Surgical resection is recommended, if possible, otherwise radiotherapy. Astonishingly, there is no information on safety margins defining R0 resection [4]. In most cases, only local excision of tumour with surrounding smooth tissue is performed which then often proves to be R1 or R2 resection. As a consequence of these incomplete resections, radiotherapy is applied in most cases. Capgar found radiotherapy to be of great importance in a study of 130 very inhomogeneously treated patients with local recurrence. However, only 25% of the patients had a complete resection of the tumour [5]. Complete chest wall resection is usually performed first after exhausting all alternative therapies [6]. In addition, many physicians consider the local recurrence as a harbinger of progressive systemic metastatic disease leading to nihilistic attitude towards further treatments. Although several reports have shown that the incidence of metastases after local recurrences is higher, the opinion that the local recurrence is a marker of metastatic formation mixes the principle of cause and effect up [7]. Fortin demonstrated that the incidence of metastases increases both after manifestation of a local recurrence and after therapy of a primary tumour after the same time. In both cases, there is a peak after about 2 years with a subsequent decrease in the incidence of new metastases [8]. Thus, the local recurrence

has to be regarded as a repeated episode of a disease with an increased risk of subsequent metastases and not vice versa. The curve of metastatic incidence might be flattened markedly by a radical resection with sufficient safety margins.

One of the most important factors is the complete resection of the tumour with sufficient safety margins of 2-5 cm. This is in most cases only possible by performing a complete chest wall resection, which almost always is possible if thoracic and plastic surgeons are cooperating. Fortin found that resection with insufficient safety margin always bears a high risk of local recurrence. Adjuvant radiotherapy did not reduce the risk (8). Treating local recurrence by resecting soft tissue solely shows a re-recurrence rate of 45% [9] to 62% (10). Radiotherapy exclusively has a re-recurrence rate of 83% [10].

Mortality after chest wall resection is reported to be 1.6%-4.5% [11]. Hospital mortality in our collective was 2%. A similar rate of 1.6% is reported by Henderson in a group of 61 patients [11]. Morbidity is reported to be 20%-50%. Faneyte described a complication rate of 40% in his collective with surgical revision being necessary in 22% [6]. A complication rate of 41% was reported by Kluiber in a group of 12 patients [12]. Our morbidity of 35% is within these ranges.

In our series following factors showed influence in predicting differences of long term survival: Age at primary treatment, tumour invasion of bony structures, additional metastases and disease free interval.

As reported by Fortin, risk factors affecting long-term survival were diameter of the local recurrence > 1.5 cm, disease-free interval < 2 years, skin invasion and initial tumour stage T2 or positive lymph nodes [8]. Faneyte found age at the time of primary resection and the disease-free interval to be prognostic factors. 5-YS in the whole collective was 45%, after R0 resection without additional metastases 58%, in the palliative setting still 21%. Patients who were less than 35 years old at the time of primary therapy had significantly lower survival rates after resection of chest wall recurrence. However, this group consists of 4 patients only, and the 5-YS is not provided [6]. Miyauchi reported on a 5-YS of 48% in 23 patients. Prognostic factors were disease-free interval and positive mediastinal lymph nodes [13]. Henderson reported on a 5-YS of only 24%. However, the incidence of incomplete resections in this group was 26%. The only prognostic factor was additional metastases [11]. The Sloan Kettering Cancer Centre reported on lymph node involvement to be a risk factor. In his group of 38 patients, Downey reported on a 5-YS of 18%. If the patients with additional metastases are excluded, 5-YS was 35%. However, this group has an astonishingly high incidence

Table 6: Literature review

Author	year	n	5-Ys	Chest wall resection	Prognostic factor
McKenna RJ [19]	1984	43	-	all	-
Miyauchi K [13]	1992	23	48%	all	DFI; mediastinal involvement
Dahlstrøm K [9]	1993	98	56%	partial	Tumor diameter, multilocular recurrence
Hathaway C [18]	1994	15		all	-
Mora EM [3]	1996	69	72%	partial	Complete resection; progression during adjuv. therapy
Faneyte IF [6]	1997	44	45%	all	Complete resection; age
Downey RJ [2]	2000	38	18%	all	Lymph node involvement; multilocular recurrence
Henderson M [11]	2001	61	24%	all	Metastases
Moran MS [20]	2002	53	55%	all	DFI
Friedel G [study at hand]	2005	51	41%	all	DFI; bone infiltration, age at the time of primary therapy

DFI: Disease free intervall

of R1 and R2 resections. Downey concludes that chest wall resection primarily represents a palliative approach [2]. Our data do not support these results. Patients with metastases, who underwent complete resection, had a 5-YS of 19.4%. We do not consider additional resection of metastases per se to be a palliative intervention. In earlier reports we have shown that metastatic resection indeed offers a curative approach in the treatment of breast cancer [14], [15], [16], [17]. Furthermore, it is recommended to always exclude metastases in view of the fact that patients with additional metastases do not profit from an extended chest wall resection. In order to obtain an adequate oncological concept a complete staging is required before starting any therapy to assess the status of the tumour disease. On the basis of these results, the adequate therapeutic approach is then selected. In most cases, however, metastatic disease does not represent a contraindication for chest wall resection.

Even in cases of multilocular metastases, resection of the local recurrence with a palliative purpose may contribute to a markedly improved quality of life. Palliative resections are mostly applied in primarily irradiated patients with a re-recurrence. Some of the tumours are ulcerated or the patients suffer from severe pain. Even in the palliative setting 5-YS rates of 21%-41.7% are reported [2], [6].

The most ostentatious prognostic factor in our group, however, was the age of women at the time of primary surgery. In contrast to the common prognosis, younger patients achieved a better prognosis by surgical therapy of the local recurrence than older patients. Whether this is really due to the therapeutic procedure or to the generally decreased life expectancy of older patients has to be subject of a more detailed investigation.

The results and the procedures of the references cited are detailed in Table 6, [18], [19], [20].

Conclusion

In locally recurrent breast cancer complete chest wall resection mostly is necessary to achieve radical resection with sufficient tumour free safety margins of 2-5 cm. To enable surgical therapy and to cover large chest wall defects cooperation between thoracic and plastic surgeon is of eminent importance.

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