Complications in Wound Healing after Chest Wall Resection in Cancer Patients; a Multivariate Analysis of 220 Patients

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Background: Extensive chest wall resections can provoke a wide variety of complications, in particular, complicated wound healing. A lower complication rate will be achieved when local factors contributing to wound healing can be identified and improved. The aim of this study is to describe these factors, irrespective of prognosis, survival, or systemic complications.

Methods: Retrospectively, the files of all patients undergoing an extended chest wall resection in a single institute during a 20-year period were retrieved. Patient demographics, use of preoperative therapy, tumor histology, the type of prosthesis (if any), and postoperative wound complications were recorded. Univariate and multivariate analysis were performed to identify factors contributing significantly to wound healing problems.

Results: From January 1987 to December 2006, 220 patients underwent a chest wall resection, defined as resection of at least one rib, and/or part of the sternum. In 145 patients (66%) this procedure was uneventful. Multivariate analysis showed that ulceration of tumor and the use of omentum for soft tissue reconstruction comprised independent factors contributing to impaired wound healing.

Conclusion: Several factors leading to wound healing problems exist preoperatively. In a multidisciplinary setting, these factors should be weighed carefully against the possible benefits of an extended chest wall resection. Especially when ulceration of a tumor exists, or when omentum is considered for soft tissue reconstruction, increased risk on wound healing problems occurs. For the majority of patients chest wall resection will remain a safe and suitable procedure.

Key Words: Chest wall resection, Complications, Breast cancer, Sarcoma, Wound healing.

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Chest wall resection (CWR) for voluminous tumors or radiation ulcers leads to soft tissue and skin loss, in combination with a skeletal chest wall defect. To reconstruct the bony skeletal lesions several artificial materials can be used. Reconstruction is necessary to preserve the rigidity of the chest wall and to prevent respiratory failure. Performing an adequate soft tissue reconstruction is a challenging problem for which several techniques of tissue transfer can be used, varying from rotation of adjacent healthy tissue into the defect, to free vascularized muscle/tissue transplants combined with a skin transplant. In patients with a persistent radiation ulcer adequate debridement of devitalised or infected soft tissue is essential before reconstruction and a prerequisite for successful and stable long-term coverage of defects.

Primary tumors of the chest wall mainly consist of sarcomas, both soft tissue and osteosarcoma. The overall 5-year survival after CWR for sarcomas is 64 to 87%.[1–3] Survival after CWR for primary malignant tumors is dependent on the histology of the tumor, the existence of free resection margins and the absence of distant metastases. Regarding the group of patients with recurrent lesions, breast cancer is the main histology instigating CWR. As can be expected, the prognosis after CWR for recurrent disease varies widely depending on the selected patient group. The overall survival at 3 and 5 years is, respectively, 41 and 18%,[4] up to a 5 years survival of 48%[5] in studies with heterogeneous patient groups.[6,7]

Despite modern techniques for chest wall reconstruction complications after this procedure are reported in 37 to 46% of patients, though published series on complication rates are of limited size, with only one publication describing more than 100 patients.[8] Reported perioperative mortality seems to be low and does not exceed 1% in larger series. The purpose of this study is to identify patient and tumor characteristics that are predictive for failure of postoperative wound healing. It will provide information concerning improvement of preoperative patient selection and the use of reconstructive techniques after CWR.

MATERIALS AND METHODS

Retrospectively, the medical files of all patients in which a CWR was performed at the department of surgical oncology of the Erasmus Medical Center/Daniel den Hoed

Cancer Center, from January 1st, 1987 to December 31st 2006, were reviewed. Included were all patients that had undergone a resection of at least one rib, and/or part of the sternum. Skeletal reconstruction of the chest wall was performed with several types of inlays during the 20 years of this study. The first few years homologous dura mater was used (Lyodura, B. Braun, Melsungen, FRG), later replaced by Polyurethane (Neurpatch, B. Braun, Melsungen, FRG) as an artificial inlay. In some cases Polyglactine (Vicryl) was used. Patients operated after 2004 received a double layer polypropylene-polytetrafluoroethylene mesh. No rigid prosthesis like plates or bone grafts were used. Standard soft tissue reconstruction was performed with an omentoplasty, unless primary closure could be established. In an earlier report operative and postoperative procedures are described in detail.[9] The preoperative data retrieved from the original patient files included patient demographics, use of preoperative chemotherapy, radiotherapy, hyperthermia, and/or doses of radiation. Furthermore, tumor characteristics including histologic type, diameter, and the presence of ulceration were retrieved from the pathology reports. Data on surgical techniques were obtained from operative reports and included the location of the chest wall lesion, the number of ribs resected, additional resections of lung parenchyma, and the methods for skeletal and soft tissue reconstruction used. Complications were graded according to the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3.0 (CTCEA 3.0, http://ctep.cancer.gov/reporting/ctc.html) and defined as perioperative if they occurred within 30 days after surgery.

This retrospective study covers a 20 years period of patient data and was not written down to describe any kind of research. It therefore does not include a statement of patient consent, neither were the operations performed in a research setting so they did not need the approval of Internal Review Boards. Complications were considered serious in case they prolonged hospital stay to over 2 weeks, in case a reoperation was needed or in case the patient died of the complication. Factors with potential prognostic value for the occurrence of complications were univariately analyzed using χ^2 tests and logistic regression. Odds ratios were estimated and 95% confidence intervals were calculated. Backward-stepwise multivariate logistic regression was performed using all factors that showed significance in the univariate analyses.

RESULTS

Patient, Tumor and Treatment Characteristics

Between 1987 and 2006, 220 patients were found meeting our definition of a CWR. There were 163 women and 57 men, with a median age of 56 years (range, 22–81 years). In Table 1 the patient's baseline characteristics and distribution of histology is shown.

In all 92 patients in the breast cancer group a CWR was performed for local recurrence. Thirty-six patients did not have any radiotherapy preceding CWR. Twenty-nine patients were treated previously with breast conserving surgery and radiotherapy. The remaining 27 patients underwent preoperative radiotherapy of the chest wall for recurrent disease, of which 16 patients received preoperative hyperthermia as well. All breast cancer patients had received some kind of systemic therapy, either hormonal, chemotherapeutical, or combinations of both. During the study period chemotherapy regimes changed several times in accordance with the national guidelines. Sixty-six patients were operated for sarcomatous tumors arising in the chest wall. Fifty-nine of these patients had primary tumors. Neither the patients with primary soft tissue sarcoma, nor the patients with recurrent disease had radiation therapy or chemotherapy before surgery. Thirty-seven patients with sulcus superior tumors were treated in a protocol including pre- and intraoperative radiotherapy. The treatment protocol of this specific group has been published before.[10] The indication for CWR of 25-patients consisted of various other types of cancer, and radiation necrosis in the absence of cancer. Preoperative ulceration of the tumor or chest wall was documented in 30 patients, almost all in patients with a history of breast cancer. In 58 patients a pedicled omentoplasty was used with a split skin graft to achieve wound closure, as described in earlier reports of our group.[11,12] Only in two cases a fasciocutaneous transposition was performed to create an appropriate soft tissue covering. In 129 patients an inlay was used as a skeletal reconstruction of the chest wall.

TABLE 1. Baseline Patient, Tumor and Treatment Characteristics of All 220 Patients

	n	%
Baseline patient, tumor characteristics		
Gender		
Female	163	74
Male	57	26
Age		
<60 yr	129	59
>60 yr	91	41
Histology		
Breast cancer	92	42
Sarcoma	66	30
Sulcus superior tumor	37	17
Others	25	11
Ulceration		
Absent	190	86
Present	30	14
Baseline patient treatment characteristics		
Pedicled omentoplasty		
Used	58	26
No indication	162	74
Use of prosthesis/inlay		
Yes	129	59
No	91	41

Complications

In Table 2 the complications imposing the most severe impact on the postoperative course are listed per patient. A complete uneventful postoperative course was seen in 145 patients (66%). Serious complications defined as resurgery ($n = 9$), prolonged stay in the hospital or readmission ($n = 28$), or death ($n = 5$) within 30 days from the operation were

TABLE 2. Complications per Patient

Complications	*n* (%)
None	145 (66)
Moderate	33 (15)
Serious	42 (19)
	n
Wound infection	24
Wound necrosis	17
Loss of inlay	9
Hemorrhage	8
Prolonged air leak	6
Pulmonary embolism	4
Empyema	3
Fistula	3
Wound dehiscence	2
Others	7
Mortality	5

seen in 42 patients (19%). In 24 patients an infection was treated with antibiotics and in three patients an empyema needed surgical drainage. Secondary wound necrosis occurred in 17 patients; in 12 patients due to more than 50% necrosis of the omentum. Loss of the artificial inlay was seen in nine patients. A logistic regression analysis of the probability of presence of complications weighed against the patient characteristics was performed.

Univariate analysis results are shown in Table 3. Significant factors in these analyses are indication for operation ($p = 0.03$), the use of omentum for reconstruction ($p < 0.001$), ulceration of the tumor ($p < 0.001$), the dose of radiotherapy >51 Gy ($p = 0.008$), and preoperative use of hyperthermia ($p = 0.002$). Multivariate analysis showed that ulceration of tumor and the use of omentum for reconstruction significantly predicted postoperative complications (Table 4).

Mortality

Five patients (2.3%) died as a result of postoperative complications. Four patients died as a result of respiratory complications, although in one of these four patients a CWR was combined with a pneumonectomy. The fifth patient underwent a large CWR for sarcoma, but died within a week from pancreatitis.

DISCUSSION

This study was performed to identify factors influencing complication rates in the surgical management of chest wall malignancies. The study focused on predictive factors for the failure of wound healing rather than on survival benefits.

Full-thickness chest wall resections leave a segment of the chest wall vulnerable to paradoxical motion during respiration. Principally, full-thickness skeletal defects are to be reconstructed with a rigid prosthesis to prevent impaired respiratory function. The decision whether or not to reconstruct the chest wall depends on the size and location of the defect and whether the wound is infected. In our experience,

TABLE 3. Univariate Logistic Regression Analyses of the Probability of Presence (Pr) of Complications

Covariate	n	Pr (%)	OR	95% CI	*p*
Tumor					0.12
Mamma carcinoma	92	42	1		
Sarcoma	66	24	0.43	0.22–0.87	
Lung; sulcus superior	37	32	0.65	0.29–1.46	
Others	25	32	0.64	0.25–1.63	
Gender					0.43
Female	163	36	1		
Male	57	30	0.77	0.40–1.48	
Age					0.39
<60 yr	129	32	1		
≥60 yr	91	37	1.28	0.73–2.25	
Indication					0.03
Curative	196	32	1		
Palliative	24	54	2.54	1.07–5.98	
Omentum					<0.001
No	162	26	1		
Yes	58	56	3.57	1.91–6.70	
Operation resection					0.47
Not limited	179	35	1		
Limited	41	29	0.76	0.36–1.60	
Sternum resection					0.20
No	183	32	1		
Yes	37	43	1.60	0.78–3.29	
Ulceration					<0.001
Absent	190	29	1		
Present	30	63	4.13	1.85–9.25	
BCT					0.24
No	171	32	1		
Yes	49	41	1.48	0.77–2.85	
Pre-CWR radiotherapy					0.09
No	140	30	1		
Yes	80	41	1.64	0.92–2.91	
Dose radiotherapy					0.008
<51 Gy	155	29	1		
≥51 Gy	65	47	2.21	1.22–4.02	
Hyperthermia					0.002
No	200	31	1		
Yes	20	65	4.13	1.57–10.86	
Pre-CWR chemotherapy					0.23
No	171	32	1		
Yes	49	41	1.50	0.78–2.88	

OR, odds ratio; CI, confidence interval; BCT, breast conserving therapy; CRW, chest wall resection.

TABLE 4. Multivariate Logistic Regression Analysis of the Probability of Presence of Complications

	OR	95% CI	*p*
Ulceration			
No/yes	2.51	1.03–6.07	0.04
Omentum			
No/yes	2.66	1.34–5.30	0.005

OR, odds ratio; CI, confidence interval.

lesions less than 5 cm in size in any location on the chest wall do not need a reconstruction. Posterior, defects up to 10 cm can be closed without prosthesis because of the overlying scapula covering the chest wall. All other defects are likely to produce a paradox chest wall motion and require a rigid reconstruction, although all rigid reconstructions should be covered with soft tissue. For this reason omentoplasties, in combination with a skin graft or (pedicled) myocutaneus flaps are often used to cover the prosthesis on complex thoracic defects. Since these soft tissue defects, especially in contaminated or irradiated fields, require well-vascularized tissue to ensure primary wound healing, the ideal flap for coverage will be thin with an abundance of tissue, pliable and well vascularized. It should also be easily accessible with minimal donor site morbidities. The omentum has been used since the 1903, when Senn[13] reported his use of the omentum as a protective wrapping for intestinal anastomoses.

We have been using omental pedicled flaps in a variety of complex thoracic defects, however, the results show that this reconstruction contributes to wound healing problems. Although described as malleable and easy to mold, caution should be taken when folding omentum; we found that especially when the omentum had been folded on itself distal flap necrosis occurred. We observed that omentoplasties covering large chest wall defects are prone for necrosis especially when postoperative infections occur.

Also the lack of structural support on the thorax rendered the omentum subject to gravitational dropping and subsequent partial necrosis. In this series, a mortality rate of 2% (5 of 220) is found, of which four patients died of pulmonary complications related to the surgical procedure. These findings are similar to the data currently available in literature (4% in 262 patients),[8] regardless of the fact that several patients described in this study underwent extensive resections. For example, in four patients an extended fore quarter amputation was performed in a palliative setting, resulting in one fatal outcome. In that specific patient the extended fore quarter amputation was combined with a pneumonectomy. In an earlier study Weyant et al.[8] describe four deaths of 9 patients in who a CWR was combined with a pneumonectomy. Clearly such an amputation can imply major complications in patients with an impaired condition.

Few prior studies have analyzed risk factors for postoperative complications after chest wall resection. Weynant has shown that size of the chest wall defect is a predictor of complications, and suggests that using rigid repair provokes less pulmonary problems. The mechanisms leading to respiratory insufficiency and failure of wound closure are weakly understood. Especially, ulcerating tumors or radionecrotic areas are at risk for postreconstructive wound healing failure. Nowadays the majority of such defects will be repaired with the use of local and regional musculocutaneous flaps, although more complicated cases require increasingly sophisticated reconstructive techniques.[14] Losken et al.[15] provide in their rapport a reconstructive algorithm following large chest wall defects with the use of vascularized flaps and prosthetic material. The risk factors included in this study were age, prior chemotherapy or radiotherapy, size of the chest wall defect, preoperative ulceration of the defect, an additional sternal or lung resection, type of prosthesis used in the reconstruction, and type of soft tissue coverage. It is demonstrated that ulceration of the tumor and covering the chest wall defect with a pedicled omentoplasty are negative factors in an uneventful postoperative course. Less convincing is the adverse role of high dose preoperative radiotherapy, whether or not in combination with hyperthermia.

This study has several limitations. First, this retrospective study covers a time period of 20 years in which surgical and radiation techniques changed in time. Advances in preoperative work-up, anesthetic care, and perioperative management will have improved outcome of these patients over years, and will continue to do so in the future. Second, comorbidity was left out of the analysis, although it is known that systemic disease like diabetes or vascular diseases can have a significant impact on wound healing.

Furthermore, comparing this data with data available in the literature is scarcely possible, since patient groups differ to a great extent. Scoring systems for complications vary widely in published studies. In 34% of our patients (75 of 220) a complication occurred of which 42 patients (19%) experienced serious complications, defined as reoperation, prolonged stay in the hospital, readmission, or death. It can be complex to draw conclusions from this data. Patient selection, surgical techniques, and the prosthesis of choice should be subject of careful consideration to prevent postoperative complications. Nevertheless from the described data it can be concluded that omentoplasty to cover the chest wall prosthesis should be avoided if possible. The choice for a myocutaneus flap, like a latissimus dorsi or transverse rectus abdominus transposition should be encouraged in future reconstructions.

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