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Inflammatory carcinoma of the breast: results of a combined-modality approach – M. D. Anderson Cancer Center experience

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Summary. A total of 106 patients with inflammatory carcinoma of the breast underwent combined-modality treatment consisting of doxorubicin-containing chemotherapy. All patients received three cycles of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) before local therapy. From 1974 to 1977 (group A), primary radiotherapy was the local treatment modality and chemotherapy was given for a total of 24 months. From 1978 to 1981 (group B), mastectomy became the primary local treatment modality and FAC was reinstituted within 10–14 days after surgery; after completion of FAC, consolidation radiotherapy was given. From 1982 to 1986 (group C), vincristine and prednisone were added to FAC, and doxorubicin was given by continuous infusion. The median follow-up of the three groups was 56 months. For patients alive at the time of analysis, median follow-ups were 141, 111, and 49 months in groups A, B, and C, respectively. Disease-free survival at 5 years was 35%, 22%, and 41% for groups A, B, and C, respectively, and respective overall survival at 5 years was 37%, 30%, and 48%. Mastectomy in addition to radiotherapy resulted in local control rates similar to those obtained with radiotherapy alone, but this approach would result in fewer late sequelae of high-dose irradiation and provided histologic staging for chemotherapy response. The patients treated on protocol C had slightly better disease-free and overall survival, but the differences were not statistically significant. The 5-year disease-free survival of patients achieving a clinical complete remission (CR) or partial remission (PR) was superior to that of patients whose response was less than a PR. There was no episode of doxorubicin-related cardiac toxicity in group C. Combined-modality treatment for inflammatory carcinoma of the breast resulted in improved survival.

Introduction

Inflammatory carcinoma of the breast is the most lethal form of breast cancer, and the prognosis is invariably grave; <10% of patients survive 5 years. Most patients die of distant metastasis with or without locoregional failure within 12–26 months [1, 10, 18, 26] if given locoregional treatment such as surgery [18, 31], radiotherapy [3], or surgery plus radiotherapy [1, 2].

For many years mastectomy was contraindicated in this disease [18, 31]. At diagnosis, it is systemic in most patients, and local therapies alone are therefore inadequate. More recently, in an effort to reduce tumor bulk maximally and to destroy occult micrometastases prior to local therapy, combined-modality approaches including systemic chemotherapy in conjunction with surgery, radiotherapy, or both have been studied. As a part of the combined-modality approach, surgical results have been encouraging, but surgery's role remains unclear [5, 6, 9, 19, 23–25, 29].

Since 1973, we prospectively studied patients with inflammatory carcinoma of the breast under three sequential treatment programs at M.D. Anderson Cancer Center. Prior to 1978, patients (group A) were treated with doxorubicin-containing induction chemotherapy, primary radiotherapy, and prolonged maintenance chemotherapy for total of 2 years [15]. From the beginning of radiotherapy until the time at which chemotherapy was reinstituted, systemic chemotherapy was interrupted for 8–10 weeks. To reduce this prolonged delay, mastectomy has been used since 1978 as the primary definitive local therapy. Radiotherapy was given for consolidation after the completion of short-term (nine cycles), doxorubicin-containing maintenance chemotherapy. In 1982, the protocol was revised, with vincristine and prednisone being added to FAC (5-fluorouracil, doxorubicin, and cyclophosphamide). The updated results obtained in these three groups of patients are presented; interim results from patients in groups A and B have previously been reported [15].

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Table 1. Treatment scheme

Protocol A	FAC, 3 cycles → Radiotherapy → FAC → CMF
Protocol B	FAC, 3 cycles → Mastectomy → FAC × 6 → Radiotherapy
Protocol C	FACVP, 3 cycles → Mastectomy → FACVP × 8 → Radio therapy

FAC: 5-fluorouracil, doxorubicin, and cyclophosphamide; FACVP: FAC + vincristine and prednisone

Patients and methods

Between May 1973 and December 1986, 106 consecutive, untreated patients with biopsy-proven inflammatory carcinoma of the breast and accompanying inflammatory signs (erythema, peau d'orange, ridging) who showed no evidence of distant metastasis were treated at M.D. Anderson Cancer Center. All patients were examined by a multidisciplinary group of physicians that included a medical oncologist, surgeon, and radiotherapist. Staging work-ups included the following: a complete history and physical examination; SMA-100 blood-chemistry analysis; complete blood, differential, and platelet counts; electrocardiography; bilateral xeromammography; liver and spleen scans or ultrasound and bone scans; and chest radiographs. Bone-marrow aspiration and biopsy, brain scans, and radiographic skeletal surveys were performed if they were clinically indicated. The patients were divided into three groups according to treatment plan, as shown in Table 1.

Combination chemotherapy consisted of FAC; three or four cycles were given to all patients during induction chemotherapy. From 1974 to 1977, 40 patients (group A) were given radiotherapy after they had received 3 cycles of FAC. The chemotherapy dose schedule included 500 mg/m^2 5-fluorouracil given i. v. on days 1 and 8; 50 mg/m^2 doxorubicin given i. v. on day 1; and 500 mg/m^2 cyclophosphamide given i. v. on day 1 of each 21-day cycle. In addition, bacille Calmette-Guérin (BCG) was given by scarification, with the upper and lower extremities being alternated on days 9, 13, and 17 of each cycle. At a total dose of 450 mg/m^2 doxorubicin, maintenance chemotherapy with cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) was then given for a total of 24 months. The maintenance program consisted of 500 mg/m^2 5-fluorouracil given p. o. on days 1 and 8; 30 mg/m^2 i. m. methotrexate on days 1 and 8; and 500 mg/m^2 cyclophosphamide given p. o. on day 2. BCG was continued on the same dose schedule.

From 1978 to 1981, tumor vaccine was added to BCG in 23 patients (group B), who underwent mastectomy after three cycles of induction chemotherapy. Within 10–14 days after surgery, chemotherapy using the same regimen was resumed. At a total dose of 450 mg/m^2 doxorubicin, chemotherapy was discontinued in group B and all patients received comprehensive irradiation. In 1982, the chemotherapeutic regimen was modified and the route of administration for doxorubicin was changed to continuous infusion over 48 h for the 43 patients in group C. Vincristine given at 1.4 mg/m^2 (maximal dose, 2 mg in patients aged <50 years and 1.5 mg in those ≥50 years of age) on day 1 and 40 mg prednisone (total dose) given p. o. on days 1–5 were added to the FAC regimen (FACVP). The total dose of doxorubicin was 550 mg/m^2 in this group. Response to induction chemotherapy was evaluated by physical examination before each cycle of therapy [21].

Primary radiotherapy with cobalt 60 and electrons consisted of an accelerated twice-daily fractionation schedule to the breast and surrounding lymphatics. In patients whose breast remained intact, 51 Gy in 40 fractions was delivered to the breast over 4 weeks using tangential portals, with each portal being treated daily. A 51-Gy tumor dose was given over 20 days to the supraclavicular and internal mammary nodes. A tangential compression boost, consisting of a 20-Gy tumor dose divided into 16 fractions, was given over 8 days to the entire breast, including the skin but not the rib cage. Oppositional boosts were delivered in twice-daily fractions to any clinically positive nodal areas (group A). Accelerated consolidation radiotherapy following mastectomy consisted of 45 Gy given over 3 weeks in 30 fractions using cobalt 60 and electrons. In addition, 5–15 Gy was delivered to the chest-wall scar and to any palpable residual nodes (groups B and C).

Table 2. Pretreatment patient characteristics

	Number of patients (%)		
	Group A	Group B	Group C
Patients (*n*)	40 (100)	23 (100)	43 (100)
Age:			
<50 years	15 (37.5)	14 (61)	17 (39.5)
>50 years	25 (62.5)	9 (39)	26 (60.5)
Race:			
White	35 (87.5)	18 (78.2)	35 (81.3)
Black	1 (2.5)	3 (13.1)	4 (9.3)
Hispanic	4 (10)	2 (8.6)	4 (9.3)
Estrogen receptor:			
<10 fmol/mg	–	8 (34.8)	20 (46.5)
>10 fmol/mg	2 (5)	6 (26.1)	10 (23.2)
Not evaluated	38 (95)	9 (39.1)	13 (30.3)
Clinical nodal involvement:			
N0	3 (7.5)	2 (8.7)	16 (37.2)
N1	7 (17.5)	9 (39.1)	9 (20.9)
N2	20 (50)	7 (30.4)	14 (32.6)
N3	10 (25)	5 (21.7)	4 (9.3)

Between 1978 and 1981, 22 patients (group B) were treated with mastectomy: 4 underwent simple mastectomy and 18 underwent extended simple mastectomy, which includes the ipsilateral lower axillary contents (level I). Since 1982 (group C), 28 patients have undergone extended simple mastectomy and 14 have had modified radical mastectomies. In each group, one patient did not undergo surgery because of rapid disease progression after three cycles of chemotherapy.

Relapse-free interval rates and survival were calculated according to the method of Kaplan and Meier [22]. Gehan's modification of the generalized Wilcoxon test was used to evaluate the differences between them [17]. Data were analyzed in July 1989.

Results

Pretreatment characteristics of 106 patients in 3 groups are shown in Table 2. In all, 12 patients did not complete the planned treatment program: 1 subject in group B and another in group C did not have local therapy because of early progression of local disease, and 5 patients each in groups B and C did not receive radiotherapy; of the latter 10, 6 developed early progression of disease prior to the initiation of radiotherapy.

The median overall follow-up was 56 months; group values were 141 months for group A, 111 months for group B, and 49 months for group C. The median age of the study population was 52 years (range, 27–78 years), with 15 (37.5%) of the patients in group A, 14 (60.9%) of those in group B, and 17 (39.6%) in group C being <50 years old. In all, 21 patients presented with clinically negative lymph nodes (NO); 25, with N1; and 60, with N2 or N3 disease. Among the 21 patients who had NO disease, 16 belonged to group C. Estrogen-receptor assay was positive in 18 cases (most were weakly positive) and negative in 28, and estrogen-receptor data were not available in 60 patients.

After induction chemotherapy and locoregional treatment, 103 of 106 patients (97.2%) were rendered free of disease; 72 patients (68%) had recurrent disease at the time of analysis. The disease-free survival is shown in Fig. 1. In all, 34% of 106 patients remained disease-free until the

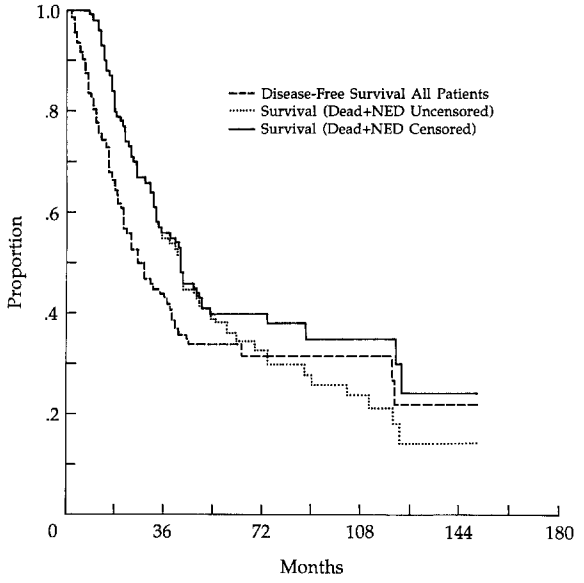

Fig. 1. Disease-free and overall survival of all patients with inflammatory carcinoma of the breast. Deaths due to other causes were either censored or uncensored. – – – –, disease-free survival of all patients; ....., survival (dead + NEd-uncensored; ———, survival (dead + NED-censored)

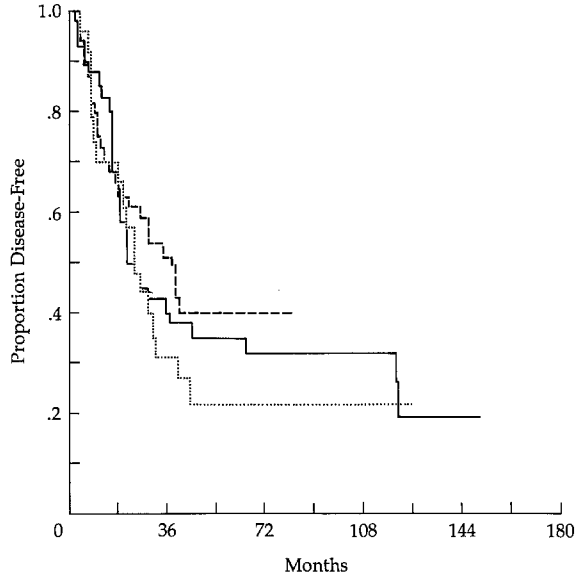

Fig. 2. Disease-free survival of patients with inflammatory carcinoma of the breast according to treatment: ———, group A (n = 40; 29 recurrences); ...., group B (n = 23; 18 recurrences); – – – –, group C (n = 43; 25 recurrences)

5-year follow-up; 35% of the patients in group A, 22% of those in group B, and 41% of those in group C were projected to be disease-free (Fig. 2) at 5 years (group A vs group B, $P = 0.787$; group A vs group C, $P = 0.384$; group B vs group C, $P = 0.211$).

The overall survival is shown in Fig. 1. A total of 32 patients were alive at the time of analysis. In all, 9 subjects died from other causes but were free of breast cancer; 3 patients died of doxorubicin-associated congestive heart disease; 2 had myocardial infarction; 1 had chronic obstructive pulmonary disease (COPD); 1 developed liver

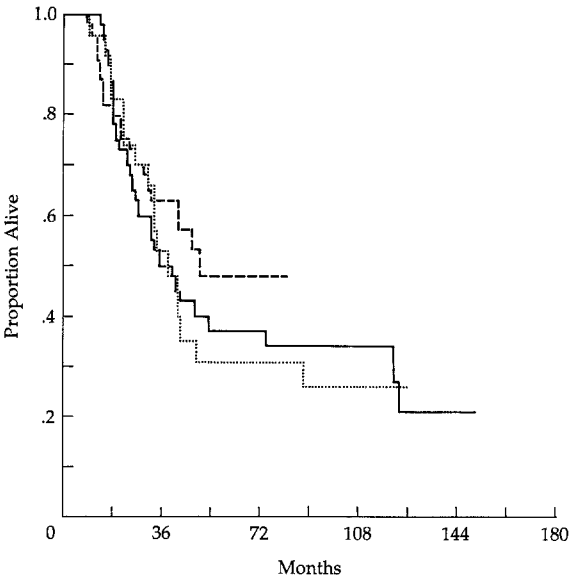

Fig. 3. Survival of all patients with inflammatory carcinoma of the breast according to treatment group. Deaths due to other causes were excluded. ———, group A (n = 40; 28 deaths); ....., group B (n = 23; 17 deaths); – – – –, group C (n = 43; 20 deaths)

Table 3. Response rates after induction chemotherapy

Response	Number of patients (%)			
	Group A[a]	Group B[a]	Group C[a]	P[b]
Complete remission	6 (15)	3 (13)	3 (8)	
Partial remission	26 (65)	10 (43)	25 (64)	0.138
Minor response	6 (15)	8 (35)	11 (28)	
No response or progression	2 (5)	2 (9)	0 (0)	
Total	40 (100)	23 (100)	39 (100)[c]	

[a] Induction chemotherapy: 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC); + FAC, vincristine and prednisone

[b] Value was calculated according to objective response (complete + partial response) rates among three groups

[c] Four patients in group C underwent mastectomy prior to chemotherapy

cirrhosis; 1, lung cancer; and 1, gastrointestinal bleeding. Overall, 40% of the patients were alive at 5 years: 37% of those in group A, 30% of those in group B, and 48% of those in group C were estimated to be alive (Fig. 3) at 5 years (group A vs group B, $P = 0.787$; group A vs group C, $P = 0.384$; group B vs group C, $P = 0.211$). The overall median survival was 44 months for all patients; group values were 39 months for group A, 38 months for group B, and 51 months for group C.

The rates of objective response to induction chemotherapy were similar in the three groups: 80% of cases in group A, with 15% in complete remission (CR); 56% of patients in group B, with 13% in CR; and 72% of cases in group C, with 8% in CR ($P = 0.138$; Table 3). Patients who achieved a CR or partial remission (PR) after three cycles of chemotherapy represented disease-free survival of 58% and 39% and overall 5-year survival of 72% and 45%,

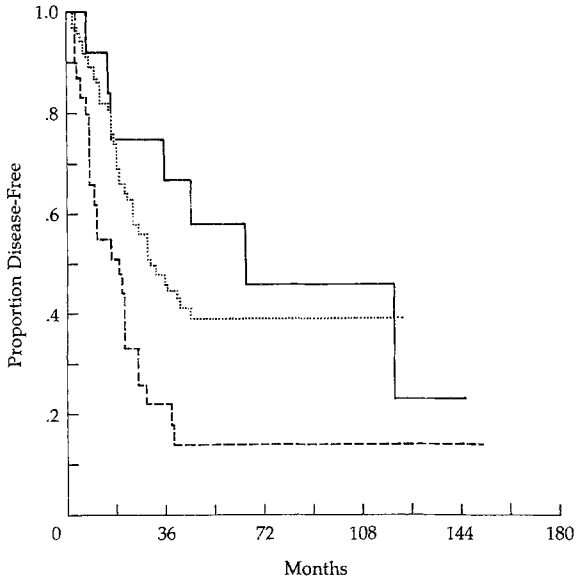

Fig. 4. Disease-free survival of all patients with inflammatory carcinoma of the breast according to response status after 3 cycles of induction chemotherapy: ———, CR (n = 12; 7 recurrences); ....., PR (n = 61; 37 recurrences); – – – –, <PR (n = 29; 24 recurrences)

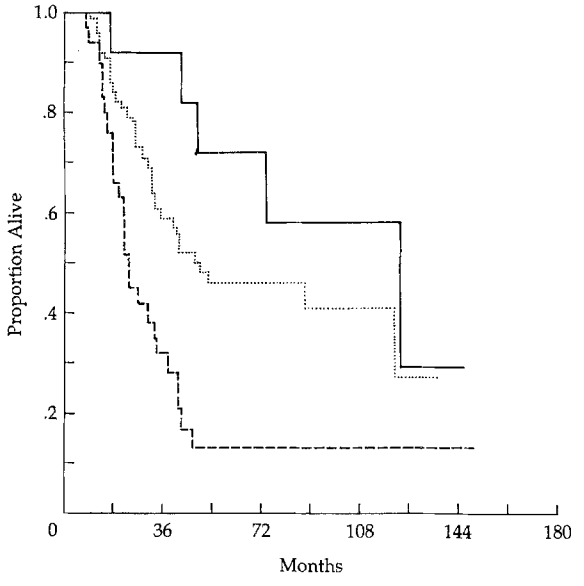

Fig. 5. Survival of all patients with inflammatory carcinoma of the breast according to response status after 3 cycles of chemotherapy. Deaths due to other causes were excluded. ———, CR (n = 12; 5 deaths); ....., PR (n = 61; 34 deaths); – – – –, <PR (n = 29; 25 deaths)

respectively. Those who achieved less than a PR had poor 5-year disease-free and overall survival (14%) (Figs. 4, 5); these differences were statistically significant (disease-free survival, P = 0.002; overall survival, P = 0.0001). In all, 37 of 60 patients (61.7%) who were ≥50 years of age and 32 of 46 (69.6%) who were <50 years old developed metastatic disease. The rates of survival according to age were similar (Table 4). Rates of disease-free and overall survival according to local therapy are illustrated in Figs. 6 and 7. There was no survival advantage for the mastectomy group (Table 4).

Table 4. Disease-free and survival rates according to prognostic factors

Prognostic factors	Patients (n)	Overall survival		Disease-free survival	
		5-year (%)	P	5-year (%)	P
Age:					
<50 years	46	43	0.5	32	0.4
>50 years	60	35		38	
Protocol:					
A (1973–1977)	40	37	0.5	35	0.6
B (1978–1979)	23	30		22	
C (1980–1986)	43	48		41	
Estrogen receptor:					
>10 fmol/mg	18	54	0.04	42	0.2
<10 fmol/mg	28	23		28	
Unknown	60	43		35	
Tumor mass on mammography:					
Yes	58	44	0.8	38	0.7
No	39	36		32	
Nodal stage:					
N0	21	40	0.7	37	0.5
N1	25	28		22	
N2	41	45		42	
N3	19	37		32	
Dermal lymphatic invasion:					
Yes	46	68	0.09	48	0.2
No	30	37		30	
Specimen not available	30	25		27	
Response to induction chemotherapy:					
CR	12	72	0.0001	58	0.002
PR	61	45		39	
<PR	29	14		13	
Mastectomy:					
No	40	41	0.6	35	0.9
Yes	66	37		32	

CR, complete remission; PR, partial remission

We assessed by pathologic examination the amount of residual tumor in surgical specimens from the 38 patients in group C, and adequate documentation regarding residual disease at surgery was obtained prospectively. In all, 4 patients (10.5%) had no residual tumor, 9 (23.7%) had minimal residual tumor (<1 cm^3), 7 (18.4%) had a moderate amount of residual tumor (1–5 cm^3), and 18 (47.4%) had extensive disease (≥5 cm^3) in their surgical specimens.

Rates of disease-free and overall survival at 5 years according to the extent of residual breast tumor are shown in Figs. 8 and 9. In all, 56% of the patients had either minimal or no residual tumor, and 58% of those who had a moderate amount of residual tumor and 17% of those who had extensive residual tumor were estimated to remain disease-free at 5 years (P = 0.028). Projected 5-year survival was 66%, 58%, and 28%, respectively (P = 0.049). Patients with estrogen receptor (ER)-positive tumors showed significantly better overall survival than those with

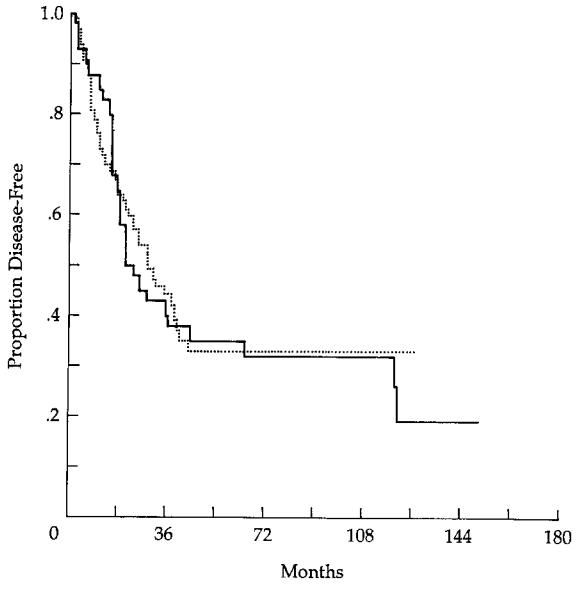

Fig. 6. Disease-free survival of patients with inflammatory carcinoma of the breast who were treated without mastectomy (group A) and with mastectomy (groups B and C) in addition to radiotherapy. ———, group A (n = 40; 29 recurrences); ....., groups B and C (n = 66; 43 recurrences)

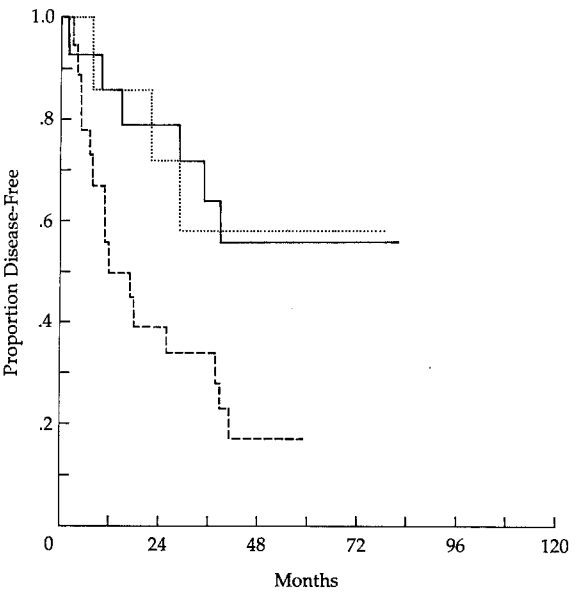

Fig. 8. Disease-free survival of 38 patients with inflammatory carcinoma of the breast according to the amount of pathologic residual tumor: ———, minimal or none (n = 14; 6 recurrences); ....., moderate (n = 7; 3 recurrences); – – – –, extensive (n = 18; 15 recurrences)

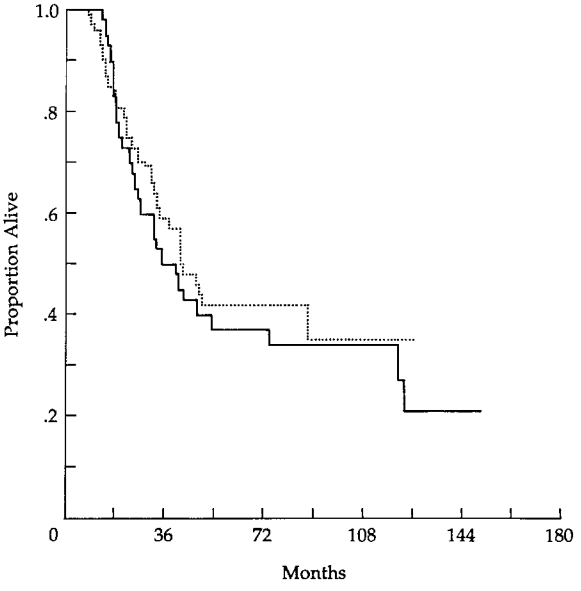

Fig. 7. Survival of patients with inflammatory carcinoma of the breast who were treated without mastectomy (group A) and with mastectomy (groups B and C) in addition to radiotherapy. Deaths due to other causes were excluded. ———, group A (n = 40; 28 deaths); ....., groups B and C (n = 66; 37 deaths)

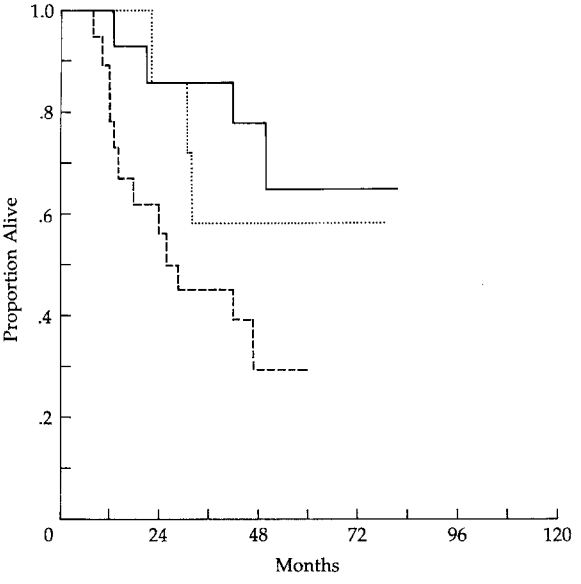

Fig. 9. Overall survival of 38 patients in group C with inflammatory carcinoma of the breast according to the amount of pathologic residual tumor. Deaths due to other causes were excluded. ———, minimal or none (n = 14; 4 deaths); ....., moderate (n = 7; 3 deaths); – – – –, extensive (n = 18; 12 deaths)

ER-negative tumors (P = 0.043), but this did not extend to disease-free survival (P = 0.199). Other factors such as the presence of tumor mass on mammography, nodal stage, and the presence of dermal lymphatic invasion had no impact on rates of disease-free or overall survival (Table 4).

Of 106 patients, 72 developed recurrent or metastatic breast cancer. The first evidence of treatment failure was locoregional in 19 patients: 7 (17.5%) in group A, 6 (26.1%) in group B, and 6 (13.9%) in group C. The rate of local recurrence in patients who underwent mastectomy in addition to irradiation (groups B and C) was 18.1% (12 of 66 cases). A total of 53 patients developed systemic recurrences: 22 (55%) in group A, 12 (52.2%) in group B, and 19 (44.2%) in group C. Recurrence developed in the viscera in 23 patients, in bone in 17 cases, in the CNS in 8 subjects, and in soft tissue in 3 cases (Table 5).

In this study, we evaluated the toxicity observed in 43 patients in group C. Most of them developed some degree of nausea and vomiting and total alopecia; grade 3 nausea or vomiting occurred in 7 cases (16.3%). Mucositis occurred in 34 subjects (79.1%), with 8 cases (18.6%) being

Table 5. Patterns of initial relapse of 72 patients who developed recurrent disease

Location	Group A ($n = 40$)	Group B ($n = 23$)	Group C ($n = 43$)
Locoregional	7 (17.5%)	6 (26.1%)	6 (13.9%)
Distant:	22 (55%)	12 (52.5%)	19 (44.2%)
Viscera	9	4	10
Bone	6	5	6
CNS	5	1	2
Soft tissue	1	1	1
Unknown	1	1	0

Values represent the number of patients; numbers in parentheses indicate the percentage of the total number of patients in each group. In all, 29 recurrences were recorded in group A; 18, in group B; and 25, in group C

>grade 3. A total of 22 patients (51.2%) developed vincristine neurotoxicity, leading to discontinuation of the drug in 6 cases (14%). There were episodes of fever in 15 patients (34.9%), 3 (7%) of whom had bacteremia; all recovered after treatment with broad-spectrum antibiotics. Of 106 patients, 6 (5.7%) developed doxorubicin-related clinical congestive heart failure (3 died as a result); all 6 had received doxorubicin by bolus. There were no episodes of doxorubicin-related heart failure in patients who were treated by continuous infusion of doxorubicin after 1982.

Discussion

Long-term follow-up data of patients with inflammatory carcinoma of the breast who were treated by the combined-modality approach at our institute are presented. This report also includes updated results previously reported for two groups of patients [19] and those of 43 patients who were treated in our last study. The results confirm the notion that combined-modality treatment has altered the natural history of this disease.

Approximately 30% of patients treated using the combined-modality approach remained free of disease, which had not been possible when patients were treated with local therapies alone. In the last study, the addition of two non-myelosuppressive drugs to the FAC regimen did not result in significantly better survival. Somewhat lower objective response rates observed in the latter subgroups of patients (groups B and C) reflected more extensive review and documentation of response by radiological studies in each patient, with clinical pathologic correlation of response.

Administration of doxorubicin by continuous infusion markedly reduced the risk of cardiotoxicity. A small fraction of patients treated in earlier groups (A and B) developed doxorubicin-related congestive heart failure, but no cardiotoxicity was found in subjects who were treated with doxorubicin by continuous infusion, despite a higher cumulative dose (group C). The duration of chemotherapy in groups B and C was reduced 9–11 cycles (23 weeks) as compared with that in group A, which underwent 24 months of chemotherapy. Patients treated in the last study (group C) demonstrated slightly better disease-free and overall survival than the other two groups, but these differences were not statistically significant.

Our patients' survival experiences were similar to those obtained in most other clinical trials using the combined-modality approach [27, 28]. This approach was also associated with a <20% risk of locoregional failure, whereas patients given radiotherapy alone had locoregional failure rates of 27%–45% [3, 4, 32]. Most patients in these studies underwent hyperfractionated irradiation, which may have also contributed to better local control [3]. Recently, Rouesee et al. [27] also observed a significant benefit of chemotherapy in both survival and locoregional control as compared with the group receiving radidotherapy alone, which showed a high local recurrence rate (31%) in a series of 230 patients with inflammatory carcinoma of the breast.

Only recently has surgery played a role in the treatment of inflammatory carcinoma of the breast [18, 31]. Zucali et al. [33] found residual tumor in 90% of mastectomy specimens after radidotherapy and reported that locally advanced breast carcinoma was not adequately treated by radidotherapy alone. A few studies have suggested that the survival of patients who are treated with combination chemotherapy and surgery in addition to radiotherapy improves over that of subjects who undergo radiotherapy alone as a local therapy [19, 29]; however, the present study using mastectomy and radiotherapy did not improve the local recurrence rate as compared with that obtained using radiotherapy alone. Mastectomy following induction chemotherapy results in significant debulking of gross residual disease, which is present in most patients; moreover, this approach avoids the higher doses of radiation that are given to patients who do not undergo mastectomy. With this approach, late complications of high-dose irradiation in patients attaining long-term survival can be prevented.

Hormonal receptor status is an important prognostic factor in breast cancer. The estrogen- and progesterone-receptor contents of inflammatory carcinoma of the breast are usually negative or weakly positive [8, 11, 20]. Controversy exists as to whether or not hormonal receptor status can affect survival in this type of breast carcinoma [8, 13, 16]. Our study suggests that overall survival is significantly better in patients with weakly ER-positive tumors than in those with negative tumors. Several authors have reported that prognostic factors such as age [7], extent of erythema or edema [9, 15, 24], initial nodal status [9, 16, 27], and dermal lymphatic invasion [14, 24] can affect survival. In our patients, there was no difference in survival according to the presence or absence of dermal lymphatic invasion and the nodal status at presentation. In our previous experience, patients who were <50 years of age had worse prognoses than those who were ≥50 years old [15], but in the present study, involving more patients, this did not prove to be the case.

For overall and disease-free survival, results were similar for all patients, regardless of age. The response to induction chemotherapy can favorably influence the course of the disease [9, 15, 20, 27]. There was no difference in response rate between the FAC- and FACVP-treated groups ($P = 0.968$). Superior 5-year disease-free survival was seen in patients who achieved a CR (58%) or

PR (39%) as compared with those who showed less than a PR (13%) to chemotherapy (relapse-free survival, $P = 0.002$; overall survival, $P = 0.0001$). However, a high percentage of our patients (31.1%) showed a very poor response to chemotherapy. For such patients, we are evaluating alternative chemotherapy in a prospective study.

Using a fixed number of chemotherapy cycles before local therapy, other investigators [12, 28] have reported similar objective response rates. Recently, Swain et al. [30] reported that a higher number of chemotherapy cycles, combined with hormonal synchronization until the achievement of a maximal objective clinical response, could attain a better response rate. These authors reported a 93% response rate, with 49% of cases achieving a CR. Although additional cycles of induction therapy resulted in a higher CR rate, the overall survival reported was similar to that obtained in other studies [30]. Although some patients treated with the combined-modality approach achieve satisfactory local control and improved survival, the majority develop distant metastasis in the course of their disease. Alternate systemic chemotherapy programs may offer a better chance of long-term control and survival in patients with inflammatory carcinoma of the breast who do not response to initial therapy. Such an approach is currently being evaluated.

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