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CLINICAL INVESTIGATION **Breast**

MANAGEMENT OF INFLAMMATORY BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Purpose: To assess the benefit of breast surgery for inflammatory breast cancer (IBC).
Methods and Materials: This retrospective series was based on 232 patients treated for IBC. All patients received primary chemotherapy followed by either exclusive radiotherapy (118 patients; 51%) or surgery with or without radiotherapy (114 patients; 49%). The median follow-up was 11 years.
Results: The two groups were comparable apart from fewer tumors <70 mm (43% vs. 33%, $p = 0.003$), a higher rate of clinical stage N2 (15% vs. 5%, $p = 0.04$), and fewer histopathologic Grade 3 tumors (46% vs. 61%, $p < 0.05$) in the no-surgery group. The addition of surgery was associated with a significant improvement in locoregional disease control ($p = 0.04$) at 10 years locoregional free interval 78% vs. 59% but with no significant difference in overall survival rates or disease-free intervals. Late toxicities were not significantly different between the two treatment groups except for a higher rate of fibrosis in the no-surgery group ($p < 0.0001$) and more lymphedema in the surgery group ($p = 0.002$).
Conclusion: Our data suggest an improvement in locoregional control in patients treated by surgery, in conjunction with chemotherapy and radiotherapy, for IBC. Efforts must be made to improve overall survival. © 2011 Elsevier Inc.

Inflammatory breast cancer, Neoadjuvant chemotherapy, Locoregional treatment, Radiotherapy.

INTRODUCTION

Inflammatory breast cancer (IBC) is defined by the International Union Against Cancer (UICC) as a clinicopathologic entity characterized by diffuse erythema and edema (peau d'orange), often without an underlying palpable mass. It is a relatively rare form (only 2% of all breast cancers in the United States) but with a dramatically increasing incidence (1–3). The management of this most aggressive form of breast carcinoma (median survival of less than 3 years) (1) has evolved over the past 3 decades (4–6). Early attempts to control disease with local treatment modalities alone, using radiotherapy (RT) with or without surgery, have had a minimal impact on survival (4), leading to the conclusion that most IBC patients have micrometastases at diagnosis. Primary chemotherapy has therefore become the mainstay of treatment and has achieved not only breast tumor regression and local control (7–10) but also improvements in survival rates (1, 10–12) (although this has been questioned by some authors (13). The current situation of relative systemic control combined with breast tumor shrinkage places new emphasis on locoregional treatment (14), and the question of the magnitude of benefit of breast surgery has not been fully elucidated (15–19). Randomized studies specifically designed to address this question are difficult to perform because of the rarity of IBC. The management of IBC is therefore based on a small number of large-scale retrospective studies that assessed the suitability of therapeutic strategies. In view of these limited data, this retrospective analysis of a large series of consecutive patients treated at the Institut Curie for nonmetastatic IBC was conducted to assess the benefit of breast surgery by comparing the outcomes of patients who underwent breast surgery after neoadjuvant chemotherapy and those who did not (exclusive RT). Special attention was also paid to the subgroup of patients with tumors showing a good response to neoadjuvant chemotherapy.

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METHODS AND MATERIALS

Patients and treatment characteristics

Between January 1 1985 and December 31 1999, of 13,180 patients diagnosed at the Institut Curie with nonmetastatic breast cancer, 280 (2%) were treated with curative intent for IBC (diffuse erythema and edema). Pathologic verification of carcinoma was always obtained either by fine needle aspiration or core biopsy before initiation of therapy. Patients were classified according to the sixth edition of the UICC guidelines (20, 21). This retrospective study was based on the 232 patients (pts) without ipsilateral supraclavicular involvement, considered along with distant metastases in previous editions of the UICC staging criteria.

Induction chemotherapy and evaluation of response

All patients received neoadjuvant chemotherapy, with a planned number of cycles of 3–6, given every 3 weeks. All patients received anthracycline, cyclophosphamide, and 5-fluorouracil (5-FU)-based chemotherapy. Sixty-six pts (28%) received high-dose sequential chemotherapy with G-CSF (granulocyte colony-stimulating factor) and repeated blood stem cell transplantation (22, 23): 7 pts (6%) in the no-surgery group and 58 pts (51%) in the surgery group. Forty-five pts (20%) received four cycles of AVCF (doxorubicin, vindesine, cyclophosphamide, and 5FU) before concomitant chemoradiotherapy (24).

One hundred thirty-three pts (57%) received concomitant chemoradiotherapy: 103 pts (87%) in the no-surgery group and 30 pts (26%) in the surgery group.

In 1997, docetaxel was introduced for a small number of patients (25), 34 pts (16%) received this agent, 3 pts (3%) in the no-surgery group, 31 pts (29%) in the surgery group.

Clinical response after induction chemotherapy was evaluated and defined according to the UICC criteria. Tumor response was assessed by either clinical (c) or imaging (i) methods using ultrasound and/or mammography and was reported as complete response (CR) when there was no palpable tumor or inflammatory signs in the breast, partial response (PR) when there was a reduction in tumor size (product of the two greatest perpendicular diameters) >50%, and minor response (MR) when the reduction was <50%. Stable disease (SD) was defined as no measurable change in the product of the two largest perpendicular dimensions, and progressive disease (PD)was defined as an increase of at least 25%.

Locoregional therapy

The dose was prescribed to mid-thickness of the breast according to the International Commission on Radiation Units and Measurements 50 recommendations (26), standard RT consisted of RT to either the whole breast (54 Gy in 27 fractions, five fractions a week) or the chest wall (50 Gy in 25 fractions, five fractions a week), followed by a boost to the tumor bed in the case of breast-conserving approaches to achieve a total dose of 70-75 Gy. Ipsilateral internal mammary chain (first three intercostal spaces) and supra/infraclavicular areas (46–50 Gy in 2 Gy per fraction) were irradiated in both groups. Axillary RT (46–50 Gy in 2 Gy per fraction) was added in the absence of axillary lymph node dissection or when this dissection showed extensive node involvement.

In the case of surgery, a major goal of the procedure was the resection of all sites of residual gross disease with negative surgical margins (>3 mm). The extent of surgery was determined by the surgeon. It ranged from conservative resection to modified radical mastectomy. The pectoral muscles were conserved. Axillary dissection was always recommended and limited to the inferior two thirds of the axilla. Because all patients who had undergone a mastectomy were referred for postmastectomy RT, immediate reconstructions were discouraged.

Locoregional treatment modalities evolved over the study period. Two main approaches can be distinguished: (*1*) exclusive RT of both the breast and regional lymph node areas (no surgery) and (*2*) breast surgery usually with locoregional RT (surgery ± RT).

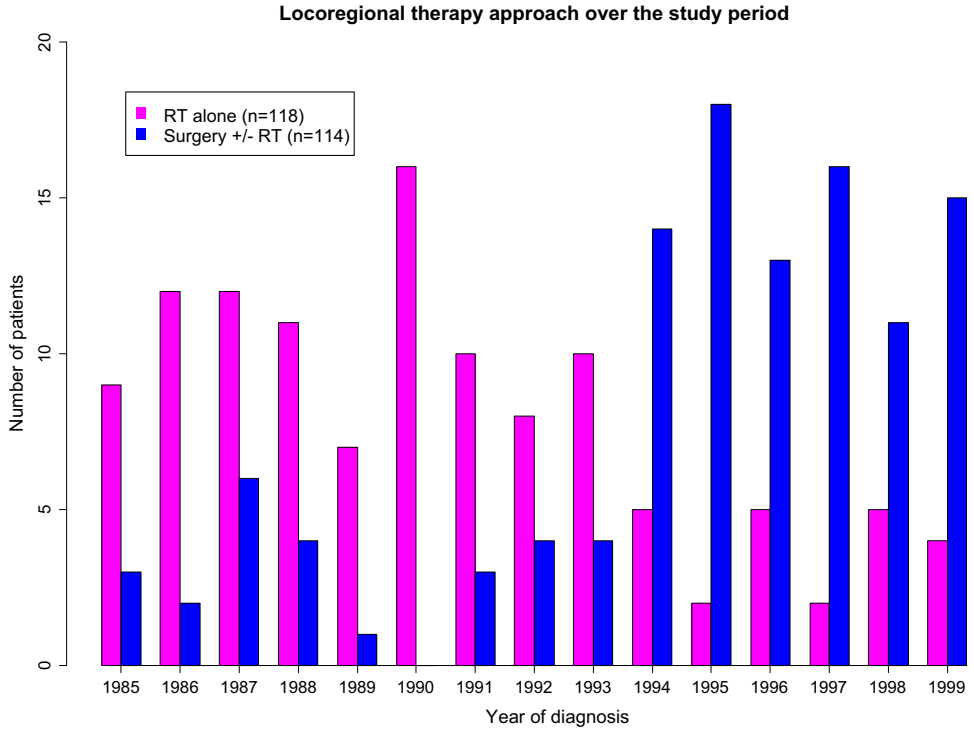

Fig. 1. Locoregional therapy approach over the study period. RT = radiotherapy.