Treatment of intraductal carcinoma of the breast with conservative surgery and radiotherapy: An Italian multicenter retrospective study

M. Amichetti,¹ O. Caffo,¹ A. Richetti,² G. Zini,³ A. Rigon,⁴ O. Lora,⁴ M. Antonello,⁵ M. Arcicasa,⁶ M. Roncadin,⁶ F. Coghetto,⁷ P. Zorat,⁷ R. Valdagni,⁸ M. Balli,⁹ G. Panizzon,⁹ S. Maluta,¹⁰ A. Di Marco,¹⁰ S. Favretto,¹⁰ N. Teodorani,¹¹ S. Neri,¹¹ S. Fasan¹²

From the Departments of Radiation Oncology of: ¹Trento, ²Varese, ³Reggio Emilia, ⁴Padova, ⁵Mestre, ⁶Aviano, ⁷Treviso, ⁸Milano, ⁹Vicenza, ¹⁰Verona, ¹¹Bologna, ¹²Venezia, Italy

A collaborative multi-institutional study on intraductal carcinoma (IDC) of the breast in twelve Radiation Oncology Departments of the north Italy was conducted. The study population comprised 206 women with IDC of the breast treated between 1982 and 1992. Surgical procedures were as follows: quadrantectomy in 158, lumpectomy in 34, and wide excision in 14 cases. The axilla was surgically staged in 141 cases: all the patients were node negative. Radiation therapy was delivered with ⁶⁰Co units (73%) or 6 MV linear accelerators (27%) for a median total dose to the entire breast of 50 Gy (mean, 49.52 Gy). The tumour bed was boosted in 137 cases at a median dose of 10 Gy. Median follow-up is 72 months. Nineteen local recurrences were recorded. All recurrent patients had a salvage mastectomy and are alive and free of disease. Actuarial overall-, cause-specific-, and recurrence-free survivals at 10 years were 93.5%, 100%, and 84%, respectively. The results of this retrospective multicentric study confirm the favourable data reported in the literature about the efficacy of breast conserving treatment of IDC with conservative surgery and adjuvant radiation therapy.

Key words: breast neoplasms; intraductal carcinoma; treatment options; treatment outcome; multicenter studies

Introduction

After its recognition in 1907, intraductal carcinoma (IDC) of the breast was rarely diagnosed, except as an incidental finding or as a palpable mass, until the 80's. During the past decade, the diffusion of mammographic screening increased the frequency of the diagnosis of IDC in a preclinical stage. Currently, IDC represents about 10% of all newly diagnosed breast cancers.

Correspondence to: Dr. Maurizio Amichetti, Ospedale Santa Chiara, Centro Oncologico, Largo Medaglie d'Oro, 38100 Trento, Italy.

UDC: 618.19-006.6-089.87-036

The treatment employed for DCIS of the breast varies widely, and the best treatment option has not yet been clearly defined. Experience with conservative management of IDC with surgery and radiotherapy (XRT) is limited in terms of both patients number reported from single Institution series and the duration of follow-up.

In this study, an analysis of 206 women with IDC of the breast treated with this conservative approach in twelve Italian institutions, is reported.

Patients and methods

A collaborative, multi-institutional retrospective study of patients affected by IDC of the breast 110 Amichetti M et al.

treated with breast-conserving therapy (excision and radiation therapy) was performed, analyzing data from 12 Institutions of the north Italy for the period 1982 to 1992.

A total of 206 sequential evaluable cases were collected. Their median age was 49 years (range 23-88 years), 92 patients had post-menopausal status; twenty-nine patients had a family history of breast cancer. Of the 126 patients with known clinical status, 103 (54%) had a palpable lump. Preoperative mammography was performed in 177 patients: 77 (43.5% of the total) were due to microcalcifications alone, 60 (34%) to mass effect alone, and 18 (10.2%) to mass plus calcification. In 112 patients a measurement of the extent of the disease in the surgical specimen was available: the median pathologic tumor size was 1.2 cm (range 0.2-5.5 cm).

The surgical treatment consisted of quadrantectomy in 158 cases, wide excision in 14, and tumourectomy in 34. An axillary dissection was performed in 141 out of 206 cases with a median of 15 lymph nodes dissected (mean 14, range 3 - 36): all the cases were pathologically negative for metastatic disease.

The tumor diagnoses were reviewed and confirmed as IDC by institutional pathologists, central pathology review being unfeasible.

The cases were classified according to the established histological criteria with respect to the dominant growth pattern; the structural features were categorized as follows: comedo (61), solid (8), cribriform (42), papillary and micropapillary (29), and cases associated with lobular carcinoma in situ (13). Irradiation with curative intent was delivered with cobalt-60 (151 cases; 73%) or 6-MV photons (55 cases; 27%), by tangential fields, encompassing the entire breast, up to doses of 45-60 Gy (mean, 49.52 Gy; median, 50 Gy) delivered in 2 Gy dose fractions in all but 2 patients. A boost consisting of an additional median dose of 10 Gy to the primary site was delivered after treatment of the whole breast in 137 cases. Neither regional nodal irradiation nor adjuvant systemic treatments were used.

Overall survival, cause-specific survival and relapse-free survival were calculated using the Kaplan-Meier method,⁴ starting from the time of surgery.

Results

The median follow-up for the group was 72 months from the date of surgery, with a range of 31-167 months. Local failure was recorded in 19

patients, at an interval of 7-109 months after surgical treatment. Ten cases were invasive carcinoma and 9 intraductal carcinoma. One patient developed an axillary nodal relapse after invasive local recurrence. No distant metastases were observed. In 12 women, both the first and the second tumors were true recurrences, occurring either at the site of previous excision or on the border of the same quadrant. Eight of the 19 patients with relapse had received a tumor-bed dose of 50 Gy, and 11 had had a supplemental external boost of 10 Gy. The initial surgical intervention had been quadrantectomy in 14 cases, tumourectomy in 4 and wide excision in one. Salvage mastectomy was performed in all the patients. One patient was also treated with adjuvant tamoxifen at the time of recurrence. All the patients with breast failure are alive without evidence of disease. None of them has subsequently failed with distant metastases.

Five- and ten-year actuarial breast recurrencefree rate is 93.5% and 84% respectively, overall survival is 98% and 93% respectively; while causespecific survival and freedom from distant metastases is 100% at five and ten years. Subsequently, 7 patients developed a contralateral carcinoma of the breast, of these 3 intraductal and 4 infiltrating.

The cosmetic outcome was separately assessed at the last follow-up in 175 cases: 87% of them had an excellent or good result.

Discussion

The surgical approach to IDC of the breast changed during the second half of the eighties by increasing use of breast conserving treatments with or without radiotherapy; thus, better cosmesis can be achieved than with mastectomy.

The results of limited surgery alone are rather unsatisfactory: local recurrence has been reported at a cumulative average rate of 19.7%, ranging from 0% to 66%, calculated from about a thousand cases reported in the literature. A comparison of these data with the reported results of conservative surgery plus definitive irradiation suggests that radiotherapy can reduce the breast cancer recurrence rate to an acceptable level but does not eliminate it. This suggests that a combination of excision and radiotherapy provides acceptable local control while ensuring excellent survival and cosmetic results.⁵⁻¹⁰

The only published randomized study is the NSABP B-17 trial¹¹ comparing limited excision fol-

lowed by irradiation or observation. There were 790 women evaluable for analysis; the addition of radiation decreased the risk of breast cancer recurrence and subsequently, the development of invasive breast cancer. The current study is the largest series of IDC treated by conservative surgery and irradiation reported in Italy. Our results are closely comparable with those reported for a series with a similar follow-up, 12-16 according to which the probability of breast preservation at 10 years was 84%. In our series cause-specific survival was 100% at 10 years, all the 19 patients with local recurrence being salvaged by mastectomy. The majority of breast recurrences in our study were observed at or near the site of primary IDC suggesting a persistence rather than a new second tumor: 12/15 known sites of recurrence were in the same quadrant as the first lesion. From these data it can be concluded that multicentric cancers rarely evolve into clinical cancer. The clinical size of the measurable palpable primary tumours in our series was relatively small, with about 80% of lesions smaller than 2 cm, and 65 patients in our study had non-palpable, mammographically discovered lesions. Recently, White et al. reported a low rate of local recurrences in patients treated by surgery and irradiation for mammographically detected lesions.8

An axillary dissection was performed in 141 patients: all the cases were pathologically negative. In the literature on conservatively treated and irradiated patients, axillary invasion was reported in 2 cases only, confirming the results reported in patients treated with mastectomy. Our study, although involving numerous Institutions, indicates that clinically or mammographically detected IDC can be successfully treated by conservative surgery and definitive irradiation.

References

- Frykberg ER, Bland KI. Overview of the biology and management of ductal carcinoma in situ of the breast. Cancer 1994; 74: 350-61.
- Lagios MD. Duct carcinoma in situ. Surg Clin North Am 1990; 4: 859-71.

- Frykberg ER, Bland KI. In situ breast carcinoma. In: Cameron JL ed. Advances in surgery. St. Louis: Mosby, 1993: 29-72 (Year Book Med Publ).
- Kaplan EL, Meier P. Non parametric estimation from incomplete observation. J Am Stat Assoc 1953; 53: 457-81.
- Silverstein MJ, Cohlan BF, Gierson ED et al. Duct carcinoma in situ: 227 cases without microinvasion. Eur J Cancer 1992; 28: 630-4.
- Forquet A, Zafrani B, Campana F, Durand JL, Vilcoq JR. Breast-conserving treatment of ductal carcinoma in situ. Semin Radiat Oncol 1992; 2: 116-24.
- Cutuli B, Teissier E, Piat JM et al. Radical surgery and conservative treatment of ductal carcinoma in situ of the breast. Eur J Cancer 1992; 28: 649-54.
- White J, Levine A, Gustafson G et al. Outcome and prognostic factors for local recurrence in mammographically detected ductal carcinoma in situ of the breast treated with conservative surgery and radiotherapy. *Int* J Radiat Oncol Biol Phys 1995; 35: 791-7.
- Warneke J, Grossklaus D, Davis J et al. Influence of local treatment on the recurrence rate of ductal carcinoma in situ. J Am Coll Surg 1995; 180: 683-8.
- Solin LJ, Kurtz J, Forquet A et al. Fifteen-year results of breast-conserving surgery and definitive breast irradiation for ductal carcinoma in situ of the breast. *J Clin* Oncol 1996; 14: 754-63.
- Fisher B, Costantino J, Redmond C et al. Lumpectomy compared with lumpectomy and radiation therapy for the treatment of intraductal breast cancer. N Engl J Med 1993; 328: 1581-6.
- Stotter AT, McNeese M, Oswald MJ, Ames FC, Romsdahl MM. The role of limited surgery with irradiation inprimary treatment of ductal in situ breast cancer. Int J Radiat Oncol Biol Phys 1990; 18: 283-7.
- Solin LJ, Fowble BL, Schultz DJ, Yeh IT, Kowalyshyn MJ, Goodman RL. Definitive irradiation for intraductal carcinoma of the breast. *Int J Radiat Oncol Biol Phys* 1990; 19: 843-50.
- 14. Mc Cormick B, Rosen PP, Kinne D, Cox L, Yahalom J. Duct carcinoma in situ of the breast: an analysis of local control after conservation surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1991; 21: 289-92.
- Sneige N, McNeese MD, Atkinson EN et al. Ductal carcinoma in situ treated with lumpectomy and irradiation: histopathological analysis of 49 specimens with emphasis on risk factors and long term results. *Hum Pathol* 1995; 26: 642-9.
- Silverstein MJ, Barth A, Poller DN et al. Ten-year results comparing mastectomy to excision and radiation therapy for ductal carcinoma in situ of the breast. Eur J Cancer 1995; 31A: 1425-7.
- Silverstein MJ, Rosser RJ, Gierson ED et al. Axillary lymph node dissection for intraductal breast carcinoma - is it indicated? *Cancer* 1987; 59: 1819-24.