original article

Breast-conserving surgery after neoadjuvant chemotherapy in patients with locally advanced cancer. Preliminary results

M. VERGINE¹, P. SCIPIONI¹, S. GARRITANO², M. COLANGELO¹, A. DI PAOLO¹, G. LIVADOTI¹, A, MATURO¹, M. MONTI¹

SUMMARY: Breast-conserving surgery after neoadjuvant chemotherapy in patients with locally advanced cancer. Preliminary results.

M. VERGINE, P. SCIPIONI, S. GARRITANO, M. COLANGELO, A. DI PAOLO, G. LIVADOTI, A. MATURO, M. MONTI

Neoadjuvant chemotherapy (NACT) in locally advanced breast tumors may allow an adequate control of the disease impossible with surgery alone. Moreover, NACT increases the chance of breast-conserving surgery. Between 2008 and 2012, we treated with NACT 83 patients with locally advanced breast cancer. We report the preliminary results evaluating the impact of NACT on the type of surgery.

KEY WORDS: Breast - Cancer - Conserving surgery - Neoadjuvant chemotherapy.

Introduction

In locally advanced breast cancers one of the goals of the neoadjuvant chemotherapy (NACT) is to convert "inoperable" tumor into "operable" tumor (1). In these patients NACT may allow an adequate control of the disease impossible with surgery alone (2). Moreover, after NACT the patients may be treated with breast-conserving surgery (3). In the presence of inflammatory or multifocal carcinoma, breast-conserving surgery is not recommended and NACT has the only purpose of increasing the survival of patients (4-10).

Patients and methods

Between 2008 and 2012, we treated a total of 1040 patients with breast cancer. Of these, 83 women were treated with NACT (Table 1). Chemotherapy schemes are anthracycline-based (until 8 cycles in responsive patients).

Results

We evaluated the results of NACT in terms of type of the subsequent surgery, i.e. conserving surgery (quadrantectomy or nipple- and skin-sparing mastectomy) versus radical mastectomy, considering the post-NACT tumor size (evaluated by imaging) as main factor in the surgical decision.

In particular (Table 1):

- in 2008, 2 out of 7 patients treated with NACT underwent to quadrantectomy and 5 patients to radical mastectomy – In the two cases treated with breast-conserving surgery following NACT the lesion was single with initial size of 3cm and a response to chemotherapy by 80% (final size < 1cm). In 3 of the 5 patients treated with radical mastectomy the initial size of the tumor was more than 5cm; in the other two patients with multifocal carcinoma the conserving surgery was not applicable;
- in 2009, 11 patients were treated with NACT: five of those underwent quadrantectomy (inclusion criteria: size reduction of 60 -70% and free margins at frozen section), while the remaining underwent to radical mastectomy;
- in 2010, 8 out of 25 patients treated with NACT underwent to conserving surgery (2 nipple- and skin-sparing mastectomy, with histological assessment of the retroareolar ducts; 6 quadrantectomy);

[&]quot;Sapienza" University of Rome, "Policlinico Umberto I", Roma, Italy

¹ Department of Surgical Sciences ² Graduate School in General Surgery (N.O.)* Coordinator: Prof. Massimo Monti

[©] Copyright 2013, CIC Edizioni Internazionali, Roma

	Patients/year, n					
	2008	2009	2010	2011	2012	
NACT (out of total)	7 (82)	11 (129)	25 (155)	17 (236)	23 (238)	
Qu	2	5	6	6	9	
NSSM	0	0	2	0	3	
RM	5	6	17	11	11	

TABLE 1 - TYPE OF SURGERY IN PATIENTS TREATED WITH NACT.

Legenda - NACT: patients treated with neoadjuvant chemotherapy; Qu: quadrantectomy; NSS: nipple- and skin-sparing mastectomy; RM: radical mastectomy.

- in 2011, 6 out of 17 patients with NACT underwent to quadrantectomy, while the remaining underwent to radical mastectomy;
- in 2012, 9 out of 23 patients treated with NACT underwent conserving surgery (3 nipple- and skinsparing mastectomy; 9 quadrantectomy).

Between 2008 and 2012, in 16 out of 50 women treated with radical mastectomy the pre-NACT tumor ranged between 2 and 4cm, and in 34 patients was > 4cm. None of the patients with initial tumor size < 2cm was treated with radical mastectomy (Table 2).

Discussion

Neoadjuvant chemotherapy is an important therapeutic approach to increase the chances of conserving surgery (11-13). NACT results in a significant clinical response in 90% of cases and complete in 25% of patients, who are histologically confirmed in 4% of cases (14, 15). If the conserving surgery is not recommended, NACT retains a crucial role for the survival of the patient (16).

Key-points for eligibility to conserving surgery are the size of the tumor (at least less than 5cm after-NACT), single and well-defined lesion, genetics (absence of mutations in the BRCA genes) (16, 17). Contraindications to conserving surgery are multifocal breast carcinoma, microcalcification spread, infiltration of the dermis, lymphatic invasion, familiarity, and lobular carcinoma (19). Patients with inflammatory carcinoma should be treated with alternative chemotherapy regimens and/or preoperative radiotherapy (18).

We preferred demolitive surgery in patients with post-NACT tumor size between 3 and 5cm, multicentric cancer, or BRCA gene mutations (20-21).

References

- Stjernswärd J. Decreased survival related to irradiation postoperatively in early operable breast cancer. Lancet 1974;2:1285.
- 2. Cuzick J, Stewart H, Peto R, et al. Overview of randomized trials

TABLE 2 - TYPE OF SURGERY BY PRE-NEOADJUVANT CHEMOTHERAPY (NACT) STAGE AND SIZE (T) OF THE TUMOR.

Pre-NACT characteristics	Years 2008-2012			
of the tumor	Qu (total 28)	RM (total 50)	NSSM (total 5)	
Stage				
IIA	10	2	3	
IIB	9	5	2	
IIIA	4	14	0	
IIIB	0	29	0	
T, cm				
0-2	16	0	4	
2.1-4	12	16	1	
4.1-5	0	34	0	

Legenda - Qu: quadrantectomy; RM: radical mastectomy; NSSM: nipple- and skin-sparing mastectomy.

Conclusion

The most clearly established advantage of neoadjuvant chemotherapy is its ability to convert patients initially ineligible for breast conserving surgery into candidate for this treatment (21).

Our preliminary results confirm that the neoadjuvant chemotherapy increases the chances of breast-conserving surgery in patients with locally advanced cancer. We believe that the key of the successful breast-conserving surgery after neoadjuvant chemotherapy are the careful patients selection and coordination among specialists.

- of postoperative adjuvant radiotherapy in breast cancer. Cancer Treat Rep 1987;71:15.
- 3. White J, Moughan J, Pierce LJ, et al. Status of postmastectomy

- radiotherapy in the United States: a patterns of care study. Int J Radiat Oncol Biol Phys 2004;60:77.
- Recht A, Gray R, Davidson NE, et al. Locoregional failure 10 years after mastectomy and adjuvant chemotherapy with or without tamoxifen without irradiation: experience of the Eastern Cooperative Oncology Group. J Clin Oncol 1999;17:1689.
- Katz A, Strom EA, Buchholz TA, et al. Locoregional recurrence patterns after mastectomy and doxorubicin-based chemotherapy: implications for postoperative irradiation. J Clin Oncol 2000;18:2817.
- Strom EA, Woodward WA, Katz A, et al. Clinical investigation: regional nodal failure patterns in breast cancer patients treated with mastectomy without radiotherapy. Int J Radiat Oncol Biol Phys 2005;63:1508.
- Schwaibold F, Fowble BL, Solin LJ, et al. The results of radiation therapy for isolated local regional recurrence after mastectomy. Int J Radiat Oncol Biol Phys 1991;21:299.
- 8. Toonkel LM, Fix I, Jacobson LH, Wallach CB. The significance of local recurrence of carcinoma of the breast. Int J Radiat Oncol Biol Phys 1983;9:33.
- Donegan WL, Perez-Mesa CM, Watson FR. A biostatistical study of locally recurrent breast carcinoma. Surg Gynecol Obstet 1966;122;529.
- Lacour J, Le M, Caceres E, et al. Radical mastectomy versus radical mastectomy plus internal mammary dissection. Ten year results of an international cooperative trial in breast cancer. Cancer 1983;51:1941.
- 11. Taghian A, Jeong JH, Mamounas E, et al. Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. J Clin Oncol 2004;22:4247.
- 12. Stefanik D, Goldberg R, Byrne P, et al. Local-regional failure in patients treated with adjuvant chemotherapy for breast cancer. J Clin Oncol 1985;3:660.

- 13. Griem KL, Henderson IC, Gelman R, et al. The 5-year results of a randomized trial of adjuvant radiation therapy after chemotherapy in breast cancer patients treated with mastectomy. J Clin Oncol 1987;5:1546.
- 14. Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. N Engl J Med 1997;337:949.
- Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. N Engl J Med 1997;337:956.
- Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet 1999;353:1641.
- 17. Mentzer SJ, Osteen RT, Wilson RE. Local recurrence and the deep resection margin in carcinoma of the breast. Surg Gynecol Obstet 1986;163:513.
- 18. Fowble B, Gray R, Gilchrist K, et al. Identification of a subgroup of patients with breast cancer and histologically positive axillary nodes receiving adjuvant chemotherapy who may benefit from postoperative radiotherapy. J Clin Oncol 1988;6:1107.
- 19. Diab SG, Hilsenbeck SG, de Moor C, et al. Radiation therapy and survival in breast cancer patients with 10 or more positive axillary lymph nodes treated with mastectomy. J Clin Oncol 1998;16:1655.
- Smith BD, Smith GL, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. J Clin Oncol 2005;23:1409.
- 21. Truong PT, Woodward WA, Thames HD, et al. The ratio of positive to excised nodes identifies high-risk subsets and reduces inter-institutional differences in locoregional recurrence risk estimates in breast cancer patients with 1-3 positive nodes: an analysis of prospective data from British Columbia and the M. D. Anderson Cancer Center. Int J Radiat Oncol Biol Phys 2007;68:59.