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APPENDIX

The other PONCAP investigators who contributed to this trial include: P. Marchi (I.N.R.C.A., Ancona), A. Reggiani (Arcispedale S. Anna, Ferrara), A. Zanollo (Ospedale Civile, Magenta), M. Pavone Macaluso (Clinica Urologica, Università di Palermo), E. Belgrano (Clinica Urologica, Università di Sassari), M. Ventura (Ospedale S. Andrea, Vercelli), D. Borin (Ospedale Generale, Stradella), F. Micali (Clinica Urologica, Università Tor Vergata, Roma), O. Gazzarini (I.N.R.C.A., Firenze), F. Pisetta (Ospedale Civile, Bolzano), P. Marchetti (Oncologia Clinica, Università dell'Aquila), P. Gallotti (Ospedale Civile, Vigevano), C. Magno (Clinica Urologica, Università di Messina), F. Cicchetti (Ospedale Bassini, Cinisello Balsamo), G. Carbone (Ospedale Garbelli, Catania), C. Giglio (Ospedali Civili, Sestri Levante).

Central Small Size Breast Cancer: How to Overcome the Problem of Nipple and Areola Involvement

Viviana Galimberti, Stefano Zurrida, Vittorio Zanini, Massimo Callegari, Paolo Veronesi, Salvo Catania, Alberto Luini, Marco Greco and Andrea Grisotti

For centrally located small tumours we have sought, with the aid of a plastic surgeon, to achieve the same radicality as in the other quadrants, while achieving a good cosmetic result. We considered 37 patients with small centrally located breast carcinoma, in whom we performed a new surgical technique. From analysis of this series it emerged that a high percentage (54.1%) had nipple and areolar involvement, suggesting their removal; it is no problem to sacrifice these when a good cosmetic result can be achieved by plastic remodelling.

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INTRODUCTION

CONSERVATIVE SURGERY plus radiotherapy has for some years been the treatment of choice for breast cancers of diameter less than 2.5 cm [1, 2]. Controlled clinical studies with up to 18 years' follow-up have shown that the incidence of local recur-

rences and of distant metastases after quadrantectomy plus axillary dissection plus radiotherapy (QUART) is similar to that after modified radical mastectomy [3–5]. Furthermore, the indications for conservative treatment, initially reserved for selected cases, have gradually expanded and, when combined

with primary chemotherapy, the treatment is now applicable to tumours of greater size [6, 7].

The standard technique was developed at the National Cancer Institute of Milan in 1973 and involves removal of a quarter of the breast with axillary lymphadenectomy in continuity or by separate incision (depending on tumour location) and subsequent radiotherapy to the remaining breast tissue. The operation is designed to achieve local radicality yet produces a good cosmetic result [8] particularly for peripherally located tumours of the upper quadrants. Retroareolar tumours and Paget's disease, on the other hand, have been treated by an inappropriately named "central quadrantectomy" involving a usually transverse, lozenge-shaped incision which removes the areola–nipple complex. This simple operation gives a poor cosmetic outcome since the mammary apex is removed to leave a flattened breast. Many surgeons in fact prefer a modified radical mastectomy in such cases, often with immediate reconstruction using a prosthesis or skin-expander.

A new technique has recently been proposed by Robles for periareolar neoplasms. This employs a periareolar excision which does not damage the areola. It provides a good aesthetic result and should ensure sufficient excision margins in healthy tissue. However, studies on removed areola–nipple large duct samples [9, 10] reveal the presence of microscopic infiltration in between 8 and 50% of instances, even when there is no clinically discernible infiltration. A factor correlating with this finding was proximity (< 3 cm) of tumour to areola. In response to this problem we have designed a new surgical approach to retroareolar and periareolar tumours, which, thanks to collaboration between an oncological surgeon and a plastic surgeon, provides adequate surgical radicality and a better cosmetic outcome.

PATIENTS AND METHODS

Patients

37 patients have undergone our modified central quadrantectomy. In all patients surgery was indicated by the presence of a neoplastic lesion in the retro or periareolar breast parenchyma. This was diagnosed clinically and mammographically in 28 cases, clinically only in 6 cases of Paget's disease, and radiologically only in 3 non-palpable cases. Patients' general data are presented in Table 1. In 34 cases pre-operative cytological investigation (28 fine needle aspirations and six scrapings) was positive for malignant tumour cells, while in the 3 non-palpable cases intraoperative histological examination (after periareolar incision) provided the diagnosis. 32 patients received homolateral axillary dissection (extending to the third level) by separate cutaneous incision. Of the 5 patients who did not receive axillary dissection, 4 had Paget's disease without evidence of nodular infiltrating lesion and 1 had infiltrating lobular carcinoma; in the latter case the small size of the lesion, lack of lymph node involvement and advanced age of the patient induced us to forego lymph node removal. The 2 remaining cases of Paget's disease underwent axillary clearance after macroscopic infiltrating carcinoma was found in the underlying breast parenchyma.

Table 1. Main characteristics of patients

No. of cases	37
Mean age	54 years
Range	36–73
Premenopausal	13
Postmenopausal	24
Site	
Right breast	19
Left breast	18
Retro	23
Peri	14
Size (mm)	
Nipple involvement	6
Non palpable lesion	5
1–10	13
11–20	10
21–30	2
> 30	1

Patients with histologically positive lymph nodes received adjuvant chemotherapy (six cyclophosphamide-methotrexate-fluorouracil cycles) if premenopausal or postmenopausal with negative hormone receptors, or hormonotherapy (tamoxifen 20 mg/day for at least 3 years) if postmenopausal and positive for oestradiol receptors (standard protocol at our institute). 34 patients received adjuvant radiotherapy, only on the operated breast, with a cobalt unit or a 5 MeV linear accelerator, beginning 3–6 weeks after surgery. Because the operation involved insertion of a rotated flap of glandular tissue into the excision space, and not direct closure, it was considered inopportune to overdose the wound. Total dose was 60 Gy to the whole breast with two opposing tangential fields and daily target dose of 2 Gy.

Surgical technique

After routine preparation of the operating field the incision line was marked on the skin. The subsequent stages were as follows.

Removal of central quadrant. A circular periareolar cutaneous incision was made and extended down to the fascia of the large pectoral muscle, so as to define and permit removal of a cone of glandular tissue, with base on the muscle, containing the tumour and a wide margin of healthy tissue. If the lesion was periareolar (within 1 cm of the areola) the removal cone was extended down asymmetrically on the lesion side.

Macroscopic examination. The removed cone of glandular tissue was sectioned serially and the sections examined to determine the size of the lesion and above all to check the adequacy of the excision margins. In Paget's disease this examination served to determine the presence or otherwise of nodular lesions in the retroareolar parenchyma.

Remodelling. A skin-glandular flap adjacent to the central quadrant was defined within the lower quadrant. The flap was de-epithelialised except for a circular area adjacent to the (removed) areola and incised along the median and inferior margins down to the fascia. The flap was then detached from the fascia, retaining a wide base. Thus mobilised, the flap was rotated upwards so as to fill the empty central quadrant, its skin island replacing the removed nipple–areola complex. Suturing was done in stages taking care that the deeper glandular layers

Correspondence to V. Galimberti.

V. Galimberti, S. Zurrada, A. Luini and M. Greco are at the Division of Surgical Oncology "B"; V. Zanini, M. Callegari and A. Grisotti are at the Division of Plastic Surgery, Istituto Nazionale Tumori, via Giacomo Venezian, 1, 20133 Milano; P. Veronesi is at the II Division of Surgery, Ospedale San Raffaele, Milano; and S. Catania is at the Division of Surgery, Ospedale Vittore Buzzi, Milano, Italy.

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Fig. 1. Sequence of steps in central quadrantectomy.

were as far forward as possible in order to completely fill the central defect and create a satisfactory cone. The flap retains its medial and lateral and part of its superior vascularisation since it is rotated from the pectoral muscle fascia, being incised along the submammary sulcus and then, vertically, from the areola to the sulcus. The type of vascularisation completed is similar to that in Strombeck's reductive mastoplasty. After closing the subcutaneous layers, cutaneous synthesis was achieved by continuous intradermal sutures. Drainage was not always necessary. Fig. 1 illustrates the sequence of operations.

Later, after the wound had healed, the breast had settled down and the radiotherapy had been completed, it was possible to simulate the areola by dermal tattooing and reconstruct the nipple using local flaps or grafts from the contralateral nipple.

RESULTS

Table 2 reports the histological diagnoses and TNM [11] classification. In 17 cases (45.9%) no microscopic infiltration of the nipple was found, while in 18 (48.7%) such infiltration was present (including the 6 Paget's disease cases). In 2 cases (5.4%) there was infiltration of the retroareolar large ducts. Of the 14 infiltrating carcinomas with microscopic involvement of the nipple and large retroareolar ducts, 10 lesions were retroareolar and 4 periareolar. In all cases the resection margins were inspected by our pathologist and reported free of disease. Axillary lymph nodes were positive in 13 patients (7 of whom received chemotherapy and 6 received hormone therapy). None of the patients suffered major side-effects from any of the treatments. Mean follow-up is 32 months (range 6–60). There have been no local recurrences nor distant metastases. One 73-year-old diabetic patient developed a local postoperative

complication: ischaemic necrosis of the skin used to cover the central defect.

The aesthetic results were evaluated by the surgeon and plastic surgeon 3 months after radiotherapy and by soliciting the opinion of the patient. The evaluation criteria were the form and symmetry of the breasts and the satisfaction of the patient. Form, considered excellent in 15, good in 19 and poor in 3 cases, was the principal objective of the remodelling. Symmetry (excellent in 11, good in 17 and poor in 9 cases) could be improved by subsequent contralateral corrective mastoplasty. Other aesthetic parameters (nipple-areola deviation, tumour site, presence of wound retraction due to en bloc axillary dissection—see for example Van Linbergen [12]) are not relevant in this series. 26 patients were satisfied with the result and 11 were not. 10 patients subsequently had nipple-areola reconstruction. Radiotherapy had no effect on the aesthetic outcome except in 1 case where it provoked mild cutaneous telangiectasy.

DISCUSSION

Microscopic involvement of the nipple-areola complex and the large retroareolar ducts has usually been studied by analysis of removed tissue from patients mastectomised for mammary carcinoma; the percentage involvement depends above all on the technique used to examine the specimens. Fisher *et al.* [13] reported 11.1% involvement in their series, Parry *et al.* [9] 8%, Smith *et al.* [14] 12.2% and Quinn and Barlow [15] 25%. Millard *et al.* [16] on the other hand maintained that microscopic involvement of the nipple was present in less than 10% of cases and this was always clinically evident as well. In the first three studies sagittal sections were taken, while Andersen *et al.* [10] found nipple and/or subareolar involvement in 20 of their 40 cases, examining horizontal sections; however, the uppermost section of the nipple was cut vertically to check for Pagetic changes. These authors considered that with sagittal sections it was easier to miss malignant foci. It has been claimed that spread to the nipple is more common when (1) the tumour is located in the central quadrant as defined by Haagensen [17]; (2) the size of the primary tumour is greater than 3 cm; (3) the nipple and areola are clinically involved and (4) the tumour is multicentric [10, 14]. Fisher noted an association between lymph node involvement and areolar involvement: when more than four lymph nodes were positive the areolar was more frequently affected.

In our 20 cases with microscopic involvement of the nipple-areola complex, this was clinically evident in only 7 (6 Paget and 1 simple skin retraction). The high percentage of our series (54.1%) with such involvement is due partially to the fact that the cases were selected for this study (small-sized tumours in the central quadrant).

Women are increasingly better informed of the need for early diagnosis in breast cancer; they know too that conservation of the breast depends on the small size of the tumour. The surgeon is, therefore, under pressure to come up with ever safer and more conservative treatments. When the tumour is in the central quadrant it is not easy to persuade the patient of the necessity for demolition (even with immediate reconstruction) just because the (small) tumour is so sited.

For centrally located small tumours we have sought to achieve the same radicality as in the other quadrants and obtain a good cosmetic result. We performed this new operation on 37 suitable breast carcinoma patients. The only difference between our

Table 2. Histological characteristics

Histological diagnosis	
IDC	16
ILC	11
Paget's disease without nodule	4
Medullar	1
IDC + DCIS	2
Paget + IDC	2
IDC + ILC	1
pTNM	
T1N0	9
T1N1	7
T2N1	1
T4N0	10*
T4N1	4
T plurifoc N0	1
T plurifoc N1	1
Paget	4

*Two Paget's with nodule. IDC, Invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma *in situ*.

technique and the traditional quadrantectomy is that the nipple-areolar dermis is excised instead of normal skin.

Our results are similar to previously published data and show that the most important predictor of nipple-areola complex involvement, other than clinical finding of such involvement, is the central location.

The requirement for conservative surgery in centrally located small size tumours has induced others to conceive incisions which allow removal of sufficient parenchyma to ensure radicality yet conserve the areola and nipple. However, the literature and our study indicate that central lesions correlate with a high incidence of involvement of the areola and nipple suggesting their removal. It is no problem to sacrifice these when a good cosmetic result can be achieved by plastic remodelling.

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The Value of Twice Yearly Bronchoscopy in the Work-up and Follow-up of Patients with Laryngeal Cancer

Luci Rachmat, Gerard C. Vreeburg, Nico de Vries, Gert-Jan Hordijk, Herman Lubsen, Johannes J. Manni and Gordon B. Snow

The aim of this retrospective study was to investigate the usefulness and feasibility of twice-yearly bronchoscopy and sputum cytology in patients with laryngeal cancer. In 170 selected patients, 500 (both initial and during follow-up) bronchoscopies were performed. There was a maximum follow-up of 34 months. 5 (2.8%) male patients developed lung cancer. In only 2 of them was the diagnosis based on bronchoscopy alone. After treatment with curative intent, both patients developed a recurrent lung carcinoma. According to most patients' experience, regular bronchoscopy is unpleasant. It is concluded that twice-yearly bronchoscopy and sputum cytology in patients with laryngeal cancer is not useful as a routine procedure. At present, chemoprevention of second primary tumours seems the most promising adjunctive treatment modality.

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INTRODUCTION

SECOND PRIMARY TUMOURS develop in 10-20% of patients with laryngeal cancer [1-8]. The majority (up to 12.5% of the total) of those second primary tumours occur in the lungs. This phenomenon is explained by the concept of "field-cancerisation"

which assumes that the whole mucosa of the respiratory tract is exposed to the same carcinogens, in particularly those in cigarette smoke and alcohol [9]. Second primary tumours and intercurrent diseases are the most important causes of death in patients with cured, early stage laryngeal cancer [10, 11]. As an adjunct to