Outcome of Immediate Breast Reconstruction in Patients With Nonendocrine-Responsive Breast Cancer: A Monoinstitutional Case-Control Study

Gaetano Aurilio,[1] Vincenzo Bagnardi,[2,3] Franco Nolè,[1] Giancarlo Pruneri,[4,5] Rossella Graffeo,[1] Jean Yves Petit,[6] Daniela Cullurà,[1] Stefano Martella,[6] Marzia Locatelli,[1] Marco Iera,[6] Piercarlo Rey,[6] Giuseppe Curigliano,[1] Nicole Rotmensz,[2] Elisabetta Munzone,[1] Aron Goldhirsch[1]

Abstract

The outcome of patients with estrogen receptor (ER)-negative breast cancer who undergo immediate breast reconstruction (IBR) after mastectomy has not been fully investigated. In the present large retrospective case-control study, in ER-negative breast cancer patients who received mastectomy, IBR was associated with a better survival trend and a lower rate of local recurrence. Extensive surgical manipulation does not affect prognosis in ER-negative patients.

Background: The long-term prognostic relevance of immediate breast reconstruction (IBR) for patients with estrogen receptor (ER)-negative breast cancer (BC) has not been fully elucidated. **Patients and Methods:** The study population included 444 patients with ER-negative BC who underwent total mastectomy with complete axillary dissection between 1995 and 2006, 339 patients with and 105 patients without IBR. The median follow-up was 8.6 years. **Results:** Patients treated with IBR were younger ($P < .001$) and received surgery more recently (2003-2006: 53.1% vs. 39%; $P = .0003$), and had a lower number of metastatic lymph nodes (>4 lymph nodes involvement: 29.5% vs. 45.7%; $P = .0026$), smaller tumors (pT1/2: 15% vs. 26.7%; $P = .0007$), and lower extent of peritumoral vascular invasion (15.9% vs. 21%; $P = .032$). The 5-year cumulative incidence of locoregional recurrence was 7.1% in the IBR group and 11.7% in the no IBR group (hazard ratio [HR], 0.81; $P = .63$). The 5-year cumulative incidence of distant metastases were similar in the 2 groups ($P = .79$). The 5-year overall and disease-free survival proportions were 79.9% versus 69.5% (HR, 1.11; $P = .67$) and 66.6% versus 54.1% (HR, 1.04; $P = .83$) in the IBR group and no IBR group, respectively. **Conclusion:** IBR intervention does not significantly affect prognosis of ER-negative BC patients.

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Introduction

Over the past 3 decades breast reconstruction after total mastectomy has progressively assumed an increasing role in the management of women with invasive breast cancer (IBC) or ductal carcinoma in situ, and delayed or immediate breast reconstruction (IBR) interventions are therefore currently used in clinical practice.

Immediate breast reconstruction is performed at the same time of total breast removal using autologous or heterologous tissue: for autologous reconstruction, local pedicle flap-based as transverse rectus abdominus myocutaneous (TRAM), latissimus dorsi or gluteal artery perforator might be valid alternatives, whereas for heterologous reconstruction expander or prosthetic implants are commonly used.

[1]European Institute of Oncology, Medical Oncology, Milan, Italy
[2]European Institute of Oncology, Division of Epidemiology and Biostatistics, Milan, Italy
[3]Department of Statistics and Quantitative Methods, University of Milan-Bicocca, Milan, Italy
[4]European Institute of Oncology, Division of Pathology and Laboratory Medicine, Milan, Italy
[5]University of Milan, School of Medicine, Milan, Italy
[6]European Institute of Oncology, Division of Plastic Reconstruction Surgery, Milan, Italy

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Address for correspondence: Gaetano Aurilio, MD, PhD, European Institute of Oncology, Medical Oncology, Via G. Ripamonti 435, 20141 Milan, Italy
Fax: +390294379234; e-mail contact: gaetano.aurilio@ieo.it

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Table 1 Demographic, Clinical, and Pathological Characteristics and Local and Systemic Treatments of the 444 Included Patients, Categorized According to Receipt of an IBR

Characteristic	Without IBR (n = 105)	With IBR (n = 339)[a]	P[b]
Year of Surgery			
1995-1999	39 (37.1)	67 (19.8)	.0003
2000-2002	25 (23.8)	92 (27.1)	
2003-2004	29 (27.6)	88 (26.0)	
2005-2006	12 (11.4)	92 (27.1)	
Age Class, Years			
<35	0 (0.0)	39 (11.5)	<.0001
35-49	19 (18.1)	166 (49.0)	
50-59	32 (30.5)	86 (25.4)	
60-69	26 (24.8)	42 (12.4)	
≥70	28 (26.7)	6 (1.8)	
Menopausal Status			
Premenopausal	19 (18.1)	199 (58.7)	<.0001
Postmenopausal	86 (81.9)	140 (41.3)	
Histotype			
Ductal	99 (94.3)	307 (90.6)	.33
Lobular	2 (1.9)	5 (1.5)	
Other	4 (3.8)	27 (8.0)	
Multicentric/Multifocal			
No	80 (76.2)	257 (75.8)	.94
Yes	25 (23.8)	82 (24.2)	
Histologic Grade			
Unknown	4 (3.8)	14 (4.1)	.14
1/2	12 (11.4)	59 (17.4)	
3	89 (84.8)	266 (78.5)	
Number of Positive Nodes			
pnX	0 (0.0)	4 (1.2)	.0026
None	41 (39.0)	133 (39.2)	
1-3	16 (15.2)	102 (30.1)	
≥4	48 (45.7)	100 (29.5)	
pT			
pT1, pTX	18 (17.1)	117 (34.5)	.0007
pT2	59 (56.2)	171 (50.4)	
pT3-pT4	28 (26.7)	51 (15.0)	
Perivascular Invasion			
Unknown	0 (0.0)	1 (0.3)	.032
Absent	54 (51.4)	203 (59.9)	
Present	22 (21.0)	54 (15.9)	
Focal	0 (0.0)	14 (4.1)	
Diffuse	29 (27.6)	67 (19.8)	
HER2 Overexpression			
Unknown	29 (27.6)	47 (13.9)	.53
Intense and complete	46 (43.8)	188 (55.5)	
Not expressed	30 (28.6)	104 (30.7)	
Ki-67			
Unknown	0 (0.0)	4 (1.2)	.87
<14%	4 (3.8)	14 (4.1)	
≥14%	101 (96.2)	321 (94.7)	
Adjuvant Local and Systemic Treatment			
Radiotherapy	28 (26.7)	108 (31.9)	.31
Chemotherapy	91 (86.7)	294 (86.7)	.99
Trastuzumab	5 (4.7)	43 (12.7)	.023

Data are presented as n (% col) except where otherwise stated.
Abbreviations: col = column; IBR = immediate breast reconstruction; TRAM = transverse rectus abdominus myocutaneous.
[a]Includes 270 prosthesis, 12 TRAM flap, 52 expander, 5 missing.
[b]Unknown are not considered in the *P* value calculation.

The choice of the reconstructive technique requires accurate consideration by a surgeon trained in various patient-related factors including host tissue condition such as breast volume, degree of ptosis, areola size, and general health status. The reconstructive success depends on coordinated planning with the oncological surgeon and careful preoperative and intraoperative management.

Immediate breast reconstruction has been reported as a safe technique without any negative effects on survival within biologically heterogeneous IBC patients.[1,2] In contrast, experimental studies have investigated the role of an extensive surgical manipulation as a potential mechanism of growth factor release, that might stimulate tumor cell proliferation and, eventually, lead to a worse outcome characterized by higher risk of locoregional recurrence.[3,4] We hypothesized that such a sequence of events might be amplified in patients with estrogen receptor (ER)-negative breast cancer (BC). This subgroup includes the basal-like and the HER2 enriched subtypes. Basal-like BC is a heavily mutated tumor associated with a high proliferation rate and a propensity to locoregional and distant metastasis, and the HER2 enriched subtype is characterized by an activation of the HER-dependent pathways leading to tumor cell proliferation and survival, and by a high rate of central nervous system metastasis. Along this line, we recently provided evidence that patients with ER-negative disease treated using neoadjuvant chemotherapy followed by surgery and IBR showed a greater risk of local relapse.[5]

To shed light on the clinical effects of IBR in the adjuvant setting, we interrogated the clinical outcome of patients who received IBR in a retrospective case-control study including a large homogeneous ER-negative early BC population.

Patients and Methods

From 1995 to 2006, a total of 444 nonendocrine responsive BC patients underwent total mastectomy and complete axillary dissection at the European Institute of Oncology in Milan. Three hundred thirty-nine patients received IBR (IBR group), and