Outcomes of Patients With Breast Cancer Who Present With Ipsilateral Supraclavicular or Internal Mammary Lymph Node Metastases

Silvia Dellapasqua,[1] Vincenzo Bagnardi,[2,3] Alessandra Balduzzi,[1] Monica Iorfida,[1] Nicole Rotmensz,[2] Barbara Santillo,[2] Giuseppe Viale,[4] Raffaella Ghisini,[1] Paolo Veronesi,[5] Alberto Luini,[6] Anna Morra,[7] Aron Goldhirsch,[8] Marco Colleoni[1]

Abstract

To evaluate outcome of breast cancer IM and SC node involvement, we evaluated 107 patients with IM or SC node involvement and a matched cohort of patients as controls. Patients with SC node involvement had a significantly poorer DFS and higher loco-regional recurrence rates compared with controls without SC node involvement.

Background: The prognostic implications of internal mammary (IM) and supraclavicular (SC) node involvement in locally advanced breast cancer is still unclear. **Patients and Methods:** We evaluated 107 patients with IM (n = 65) or SC (n = 42) node involvement who underwent operation at the European Institute of Oncology between 1997 and 2009 to assess their prognostic features. We subsequently analyzed matched cohorts, using the 107 patients as cases and another group of patients as a control cohort, to evaluate prognostic differences between patients with and those without IM or SC node involvement. **Results:** Five-year disease-free survival (DFS) was 84% in IM vs. 38.8% in SC node involvement ($P < .0001$), and 5-year overall survival (OS) was 96.9% in IM node vs. 57.1% in SC node involvement ($P < .0001$). No difference in outcome was found between patients with and controls without IM node involvement. Conversely, a statistically significant difference in DFS and locoregional recurrence was observed in patients with SC node involvement compared with controls without SC node involvement. **Conclusion:** SC node involvement correlated with a significantly poorer outcome in patients with locally advanced breast cancer. Adequate staging, including biopsy of suspicious locoregional ipsilateral lymph nodes, is mandatory in these patients. Patients with IM or SC node involvement should be treated with curative intent using combined-modality treatments.

Introduction

The precise prognostic significance of internal mammary (IM) chain and supraclavicular (SC) lymph node involvement in patients with locally advanced breast cancer is still debated, and therapeutic choices in patients in whom IM or SC lymph nodes (or both) are involved are still not uniformly defined.

The IM lymph node chain is represented by a variable number of lymph nodes (average of 6) situated behind the intercostal muscles and costal cartilages. The nodes are generally located close to the IM vein and artery, and more often in the first, second, and third spaces. The first surgeon who explored the intercostal spaces was Handley in 1922[1] who found metastatic IM nodes in 4 of 6 patients. He suggested that radiotherapy should be applied to the parasternal region in patients with breast cancer. A series of 100 cases treated with IM node removal was published in 1959 by Bucalossi and Veronesi, showing the poor prognosis of patients with

[1]Division of Medical Senology, European Institute of Oncology, Milan, Italy
[2]Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan, Italy
[3]Department of Statistics and Quantitative Methods, University of Milan-Bicocca, Milan, Italy
[4]Division of Pathology and Laboratory Medicine, European Institute of Oncology and University of Milan, Italy
[5]Integrated Breast Surgery Unit, European Institute of Oncology and University of Milan, Italy
[6]Division of Senology, European Institute of Oncology, Milan, Italy
[7]Division of Radiation Oncology, European Institute of Oncology, Milan, Italy
[8]Department of Medicine, European Institute of Oncology, Milan, Italy

Table 1 Baseline Characteristics of Patients With SC or IM Node Metastases and Matched Groups

	Patients by Type of Node Metastasis Group						
	Internal Mammary (n = 65)	Control Group (n = 65)	P Value[a]	Ipsilateral Supraclavicular (n = 42)	Control Group (n = 42)	P Value[b]	P Value[c]
Variable	n (%)	n (%)		n (%)	n (%)		
Matching Variables							
Neoadjuvant therapy			—			—	<.0001
No	56 (86.2)	56 (86.2)		13 (31)	13 (31)		
Yes	9 (13.8)	9 (13.8)		29 (69)	29 (69)		
Year of surgery			—			—	<.0001
Before 2000	0 (0)	3 (4.6)		11 (26.2)	6 (14.3)		
2000-2003	27 (41.5)	28 (43.1)		24 (57.1)	25 (59.5)		
2003-2006	23 (35.4)	13 (20)		3 (7.1)	6 (14.3)		
2007-2009	15 (23.1)	21 (32.3)		4 (9.5)	5 (11.9)		
Age (years)			—			—	.007
<35	4 (6.2)	3 (4.6)		2 (4.8)	2 (4.8)		
35-50	35 (53.8)	35 (53.8)		9 (21.4)	11 (26.2)		
51-65	21 (32.3)	21 (32.3)		25 (59.5)	26 (61.9)		
>65	5 (7.7)	6 (9.2)		6 (14.3)	3 (7.1)		
Positive lymph nodes at surgery (n)			—			—	<.0001
None	1 (1.5)	1 (1.5)		7 (16.7)	7 (16.7)		
1-3	33 (50.8)	33 (50.8)		4 (9.5)	4 (9.5)		
4-9	14 (21.5)	14 (21.5)		6 (14.3)	6 (14.3)		
10+	17 (26.2)	17 (26.2)		25 (59.5)	25 (59.5)		
pT status			—			—	<.0001
pT0	1 (1.5)	1 (1.5)		6 (14.3)	6 (14.3)		
pT1	25 (38.5)	25 (38.5)		10 (23.8)	10 (23.8)		
pT2	30 (46.2)	30 (46.2)		9 (21.4)	9 (21.4)		
pT3-4	9 (13.8)	9 (13.8)		17 (40.5)	17 (40.5)		
Tumor subtype			—			—	.002
Luminal A	11 (16.9)	13 (20)		2 (4.8)	8 (19)		
Luminal B (Ki67 ≥14)	38 (58.5)	38 (58.5)		11 (26.2)	10 (23.8)		
Luminal B (HER2+)	8 (12.3)	7 (10.8)		3 (7.1)	3 (7.1)		
HER2+	3 (4.6)	2 (3.1)		7 (16.7)	4 (9.5)		
Triple negative	4 (6.2)	4 (6.2)		8 (19)	8 (19)		
NA	1 (1.5)	1 (1.5)		11 (26.2)	9 (21.4)		
Other Prognostic Factors							
Histologic type			.060			.128	.918
Negative	0 (0)	1 (1.5)		2 (4.8)	2 (4.8)		
Ductal	54 (83.1)	44 (67.7)		32 (76.2)	27 (64.3)		
Lobular	3 (4.6)	11 (16.9)		2 (4.8)	8 (19)		
Other	8 (12.3)	9 (13.8)		6 (14.3)	5 (11.9)		
Grade			.501			.004	.001
Unknown	11 (16.9)	12 (18.5)		26 (61.9)	33 (78.6)		
1-2	35 (53.8)	31 (47.7)		3 (7.1)	7 (16.7)		
3	19 (29.2)	22 (33.8)		13 (31)	2 (4.8)		
PVI			.129			.387	.850
Absent	28 (43.1)	35 (53.8)		18 (42.9)	21 (50)		
Present	10 (15.4)	13 (20)		5 (11.9)	3 (7.1)		
Focal	3 (4.6)	5 (7.7)		1 (2.4)	4 (9.5)		
Diffuse	24 (36.9)	12 (18.5)		18 (42.9)	14 (33.3)		