Axillary Dissection May Not Be Needed In Early-Stage Breast Cancer with Clinically Negative Axilla- Cohort Prospective Study

Abstract

Introduction: Over many years breast cancer is managed by surgery to the primary tumor site and complete surgical axillary dissection. The last is done for proper axillary staging … and may improve the locor-egional recurrence and overall survival. Axillary LN dissection is associated with many complications and morbidity, especially lymphedema. When SLN was introduced to the field of breast cancer management, it greatly decreased the need for axillary dissection and its sequela. In areas like our locality (Iraq-Basrah governorate), the SLN procedure is not available. Avoiding axillary dissection in a breast cancer patient with a clinically negative axilla is a challenging one for the patient who is afraid of avoiding such surgery and the relevant doctors who are not sure about its safety as the relevant studies about this issue are few. In this study, we will assess the management of early-stage breast cancer and clinically negative axilla with primary breast surgery and adjuvant treatment (chemotherapy and radiotherapy, and hormonal treatment according to the indications) only without axillary dissection and compare them with a similar group of patients with axillary dissection.

Aim of the study: To answer the question: is the omission of the axillary LN dissection safe in early-stage breast cancer with clinically negative axilla?

Patients and methods:

Study design

This is a single-center cohort study. Involves 97 females aged ≥18 years with histologically confirmed invasive breast cancer stage I-II-III, with clinically negative axillary lymphadenopathy (by clinical examination, ultrasound, CT scan +_ PET scan). SLN was not done (unavailable). Out of those patients, 48 females had undergone surgery (mastectomy or BCS) without axillary surgery and the remaining females had primary breast surgery with axillary lymph node surgical assessment. All the patients were treated with surgery to negative margins (no tumor at ink), followed by adjuvant systemic therapy (including hormonal treatment for five years for hormone receptor-positive disease), followed by whole breast opposing tangential field RT. Patients were kept under regular follow-up for 3 years for assessment of disease recurrence according to the recommended clinical practice. History and physical exams were performed every very 3–4 months in the first 2 years, and every 6–8 months from years 3 to 5 thereafter (ESMO Guideline). Annual mammography was performed; other testing was directed by the patients' symptoms and the discretion of the treating physician. Regular pelvic ultrasound was performed twice yearly for a patient on adjuvant tamoxifen.

Primary end-point: The main comparative assessment was the progression-free survival between the two groups. Progression-free survival is defined as the period from diagnosis of breast cancer until the loco-regional progression (axillary, internal mammary, supraclavicular or sub-clavicular LAP), distant metastasis, or death. In addition, we assessed the other adverse events like lymphedema between the groups over 3 years.

Exclusion criteria: We excluded patients with distant metastasis, and those who refused to be included in the study (the main cause was fear of locoregional recurrence).

Statistical analysis: Statistical calculations were done using Statistical Package for the Social Sciences version 25 (SPSS Inc.). In which categorical data were expressed as numbers and percentages, and the differences between the groups were analyzed using the Chi-square test (X2) and Fisher exact test. Continuous data expressed as mean± SD and the differences between the groups were analyzed by the Independent sample T-test for normally distributed data. Shapiro-Wilk test was used to test the normality of the data, and outliers were detected using Boxplot methods. The confidence interval of 95% was applied as the dependent interval in statistics and P-values <0.05 were accepted as statistically significant.

Results: The study included a total of ninety-nine patients diagnosed with breast cancer. There were no significant differences in the mean age of both Group I (patients had no history of axillary dissection) and Group II (patients underwent axillary dissection surgery) ($p=0.861$), also no significant differences were observed between the studied groups regarding the past medical history ($p=0.205$). The study showed significant differences between Group I and Group II in terms of the grade of carcinoma ($p=0.008$), most of the Group I had a grade II cancer (70.8%) followed by grade III (29.2%), meanwhile, most of the Group II were grade II (90.2%) followed by grade III and grade I (7.8%), (2.0%) respectively. The type of surgery was as well significantly different between Group I and Group II ($p<0.05$).

Table 1. Comparison between Group I and Group II regarding the demographical parameters.

Variables		Group I (No. 48)	Group II (No. 51)	P-value
Age (years) (mean± SD)		47.54± 12.048	47.96± 11.672	0.861⸸
Past medical history	No	40 (83.3%)	37 (72.5%)	0.205⸎
	Asthma	0 (0.0%)	1 (2.0%)	
	Diabetes mellitus	1 (2.1%)	1 (2.0%)	
	Diabetes mellitus and hypertension	3 (6.3%)	4 (7.8%)	
	Diabetes mellitus, hypertension, and ischemic heart disease	0 (0.0%)	1 (2.0%)	
	Hypertension	2 (4.2%)	6 (11.8%)	
	Hypothyroidism	1 (2.1%)	1 (2.0%)	
	Tuberculosis	1 (2.1%)	0 (0.0%)	
Grade	**I**	0 (0.0%)	1 (2.0%)	0.008*⸎
	II	34 (70.8%)	46 (90.2%)	
	III	14 (29.2%)	4 (7.8%)	
Type of surgery	Lumpectomy	44 (91.7%)	28 (54.9%)	<0.05*‡
	Mastectomy	4 (8.3%)	23 (45.1%)	

‡ Pearson X^2 test ⸸ Independent t-test ⸎ Fischer's exact test * Significant at P-value < 0.05

The study showed no significant differences between the Group I and Group II in terms of chemotherapy (p=0.554), in which (93.7%) of the Group I received chemotherapy while (6.3%) either did not or refused to receive chemotherapy, however, all the Group II received chemotherapy. Regarding radiotherapy, the study showed significant differences between the Group I and Group II (p=0.009), in which most of Group I and Group II received radiotherapy (93.8%), (82.4%)) respectively, while (6.3%) of Group I either did not or refused to receive radiotherapy, however, (17.9%) of Group II did not receive radiotherapy.

Table 2. Comparison between Group I and Group II regarding the treatment regimen.

Variables		**Group I (No. 48)**	**Group II (No. 51)**	**P-value**
Chemotherapy	No	1 (2.1%)	0 (0.0%)	0.554ǂ
	Refused	2 (4.2%)	0 (0.0%)	
	AC - T Neo Adjuvant	3 (6.3%)	0 (0.0%)	
	AC –T	28 (58.3%)	36 (70.6%)	
	AC * 6	5 (10.4%)	4 (7.8%)	
	AC *4	0 (0.0%)	1 (2.0%)	
	Default	1 (2.1%)	1 (2.0%)	
	FEC – T	2 (4.2%)	3 (5.9%)	
	TAC *6	1 (2.1%)	1 (2.0%)	
	TC * 4	5 (10.4%)	5 (9.8%)	
Radiotherapy	Yes	45 (93.8%)	42 (82.4%)	0.009*ǂ
	No	1 (2.1%)	9 (17.6%)	
	Refused	2 (4.2%)	0 (0.0%)	

ǂ Fischer's exact test

***** Significant at P-value < 0.05

The current study showed no significant differences between Group I and Group II in terms of loco-regional metastasis (p=0.614), where (10.4%) and (13.7%) of the Group I and Group II had loco-regional metastasis. Out of those with loco-regional metastasis, most of the Group I was metastasized to the axillary and systemic nodes (4.2%) and (2.1%) to the nodes of the ipsilateral shoulder, however, all Group II had a local metastasis (9.8%). In terms of distant metastasis, no significant differences were observed between Group I and Group II (p=0.527), where only (22.9%) and (19.6%) of both Group I and Group II had distant metastasis. Among those who had metastasis (4.2%) of the Group I were showed metastasis to the bone, lung, brain, and liver while (2.1%) were metastasized to the sternum, while control patients showed (5.88%) were metastasized to the bone and (11.8%) to the lung with (1.96%) were metastasized to the brain and liver.

Lymphedema was as well not statistically significant between Group I and Group II (p=0.571), in which only (8.3%) of Group I and (11.8%) of Group II had lymphedema while (91.7%) of Group I and (88.2%) of Group II did not have any lymphedema.

Table 3. Comparison between Group I and Group II regarding the loco-regional and distant metastasis.

Variables		Group I (No. 48)	Group II (No. 51)	P-value
Loco regional metastasis	Yes	5 (10.4%)	7 (13.7%)	0.614‡
	No	43 (89.6%)	44 (86.3%)	
	Axillary and systemic recurrence	2 (4.2%)	0 (0.0%)	0.28⋕
	Ipsilateral shoulder	1 (2.1%)	0 (0.0%)	
	Local	0 (0.0%)	5 (9.8%)	
Distant metastasis	Yes	11 (22.9%)	10 (19.6%)	0.527‡
	No	37 (77%)	41 (80.4%)	
	Bone	2 (4.2%)	3 (5.88%)	0.956⋕
	Lung	2 (4.2%)	6 (11.8%)	
	Brain	2 (4.2%)	1 (1.96%)	
	Liver	2 (4.2%)	1 (1.96%)	
	Local	1 (2.1%)	0 (0.0%)	
	Sternum	1 (2.1%)	0 (0.0%)	
Lymphedema	Yes	4 (8.3%)	6 (11.8%)	0.571‡
	No	44 (91.7%)	45 (88.2%)	

‡ Pearson X^2 test.
⋕ Fischer's exact test

Conclusion: No significant differences were seen in the Loco regional metastasis, and distant metastasis between the two groups, lymphedema was low among those without axillary dissection, although loco regional recurrences were higher in the group with axillary dissection.