Complications of Axillary Lymph Node Dissection in Treatment of Early Breast Cancer: A Comparison of MRM and BCS

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Abstract ALND is part of primary management of breast cancer. In spite of complications it causes, its use in prognostication and planning adjuvant treatment in carcinoma breast is unquestioned. Prospective study was conducted on 100 patients of EBC [clinical stage I&II]. 50 underwent MRM, 50 WLE&AC. Patients were asked to rate on likert scale various symptoms on follow up. Multivariate regression analysis was carried out between pain, numbness, limitation of shoulder or arm motion, arm swelling, infection and age, BSA, clinical status of axilla, no. of LNs removed, no. of positive LNs, co-morbidities, chemotherapy, radiotherapy, hormone therapy, type of surgery. 60% patients reported one or more symptoms. Numbness, pain were reported by 39% each, arm swelling by 25%, limitation of arm movement by 16%, infection by 11%. Symptoms were mild in majority. On regression analyses numbness was associated with EBRT, co-morbidity, type of operation (p value- <0.01 , <0.01 , <0.05), pain had no significant association, swelling with EBRT, no. of LNs positive for metastases, co-morbidity, type of operation (p value- <0.01 , <0.05 , <0.05 , <0.01), limitation of arm motion with no. of positive LNs (p value- <0.01), infection with no. of positive LNs, co-morbidity (p value <0.05 , <0.05). There was no statistically significant

difference in reporting of symptoms by patients in two groups. ALND caused morbidity in majority of patients but few reported severe symptoms and interference with daily activities.

Keywords Breast cancer · Complications · Axillary lymph node dissection · Treatment

Introduction

Early breast cancer [EBC] constitutes 30% of breast cancer cases seen at regional cancer centres in India [1]. Axillary lymph node dissection [ALND] is the gold standard in evaluation of axillary lymph node metastases and is an integral part of the treatment of breast cancer. It provides benefit for breast cancer patients by rendering regional control and may improve overall survival by surgical removal of microscopic nodal metastases [2]. Because of wide array of treatment options available today, the number of positive lymph nodes have important implications in choosing the right treatment strategy (Figs. 1 and 2, Tables 1 and 2).

The use of ALND is questioned in recent years, controversy arises because of inherent morbidity following ALND without directly contributing to survival [3]. Complications after surgery for breast carcinoma include lymphedema of the arm, numbness of arm and chest wall, restriction of movement of arm, pain and infection in arm and chest wall [4–6]. Because of this morbidity following routine ALND, various alternatives have been advocated like axillary sampling [7], limited level I dissection [8, 9] and sentinel lymph node biopsy [10].

While a number of studies have objectively measured morbidity from axillary clearance [6, 11–13], few studies

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Fig. 1 Distribution of patients according to different symptoms on Likert scale

have addressed patients' subjective assessment of the problems resulting from modified radical mastectomy [MRM]/breast conserving surgery [BCS] [3].

Contradictory results have been shown by various studies which have compared complications and quality of life [QOL] after MRM and BCS. One study showed no difference [14] while the other found that women who underwent BCS experienced greater psychological distress and marginally worse QOL [15], while another reported better QOL for patients undergoing BCS [16]. Pain and arm symptoms were also reported to be higher in the BCS group by various studies [16, 17], while others reported higher incidence in the MRM group [18].

The aim of the present study was to know the incidence and severity of the complications of ALND in patients undergoing MRM/BCS by patient survey.

Materials and Methods

A prospective study was carried out at Mohan Dai Oswal Hospital [MDOH], Ludhiana on 100 female patients of early breast cancer i.e., clinical stage I and II [according to AJCC 5th edition], between August 2004 to August 2006. Patients in the age group of 20–65 years were included in the study. Patients <20 years and >65 years, patients with bilateral disease, disease recurrence and refusal to participate in the study were excluded. Patients were planned for MRM or WLE&AC depending upon the site of tumor, size of tumor in relation to breast size and patient's desire. Patients were divided into two groups:

- Group 1. Patients who underwent MRM
- Group 2. Patients who underwent wide local excision and axillary clearance [WLE&AC]

Fig. 2 Distribution of subjects according to pathological TNM staging (UICC 6th edition)

Table 1 Distribution of subjects according to lymphnode metastases

Nodal Status	Menopausal Status	MRM		WLE & AC		Total	
		No.	%age	No.	%age	No.	%age
Nodes Negative	Pre	5	26.31	17	60.00	22	22.00
Nodes Positive:<4LN	Pre	10	52.63	7	25.00	17	17.00
Nodes Positive:> = 4LN	Pre	4	21.05	4	14.28	8	8.00
Nodes Negative	Post	15	48.38	14	63.63	29	29.00
Nodes Positive:<4LN	Post	12	38.70	3	13.63	15	15.00
Nodes Positive:> = 4LN	Post	4	12.90	5	22.72	9	9.00

All surgeries were performed in a one surgical unit. MRM was done by Auchin Closs method employing a transverse elliptical incision. Axillary clearance was done

up to level III in all cases. Intercostobrachial nerves were excised in majority of the cases. Long thoracic nerve, thoracodorsal bundle and axillary vein were identified and preserved in all cases. Electrocautery was used in all the cases.

Table 2 Distribution of patients according to different symptoms

Symptoms	MRM		WLE & AC		Total	
	No.	%age	No.	%age	No.	%age
Numbness						
0	31	62.00	30	60.00	61	61.00
1	9	18.00	14	28.00	23	23.00
2	9	18.00	4	8.00	13	13.00
3	1	2.00	2	4.00	3	3.00
4	—	—	—	—	—	—
5	—	—	—	—	—	—
<i>p</i> -value	>0.10 ns					
Pain						
0	29	58.00	32	64.00	61	61.00
1	13	26.00	17	34.00	30	30.00
2	6	12.00	1	2.00	7	7.00
3	2	4.00	0	0.00	2	2.00
4	—	—	—	—	—	—
5	—	—	—	—	—	—
<i>p</i> -value	>0.10 ns					
Swelling						
0	34	68.00	41	82.00	75	75.00
1	11	22.00	5	10.00	16	16.00
2	3	6.00	4	8.00	7	7.00
3	2	4.00	0	0.00	2	2.00
4	—	—	—	—	—	—
5	—	—	—	—	—	—
<i>p</i> -value	>0.10 ns					
Limited Motion						
0	39	78.00	45	90.00	84	84.00
1	8	16.00	4	8.00	12	12.00
2	2	4.00	1	2.00	3	3.00
3	1	2.00	0	0.00	1	1.00
4	—	—	—	—	—	—
5	—	—	—	—	—	—
<i>p</i> -value	>0.10 ns					

In WLE&AC separate incisions were employed for lump excision and axillary dissection.

Axillary clearance was done upto level III by an incision 2.5 cm below the axillary line.

In the post operative period all patients were instructed to perform the arm exercises to maximize the range of shoulder movements.

Patients were given adjuvant treatment depending upon the size of tumor, lymph node positivity, type of surgery, hormone receptor and menopausal status.

The patients were followed up in OPD after completion of their adjuvant treatment. During their follow up visits they were asked to fill up a questionnaire rating their symptoms of arm numbness, pain in arm and chest wall, restriction of movement of shoulder and infection episodes in arm and chest wall on a 5 point likert scale. On the likert scale scores of 1–2 indicated mild symptoms, 3–4 indicated moderate symptoms and 5 indicated severe symptoms. The time between surgery and filling of questionnaire by the patients ranged from 6 months to 2 years.

Medical records of patients were also analyzed for age, menopausal status, clinical presentation, duration of symptoms, side affected, quadrant, size of breast lump, axillary lymphadenopathy, clinical staging, histopathology report [type of tumor, grade of tumor, number of lymph nodes removed, number of lymph nodes positive for metastasis], histopathological stage, estrogen and progesterone receptor status, her-2-neu positivity and adjuvant treatment received.

Logistic regression analyses was carried out to determine the correlation between the response variables [pain, numbness, arm movement limitation, arm swelling and infection], and predictor variables [age, body surface area {BSA}, clinical status of axilla at presentation, type of surgery, number of lymph nodes removed, number of positive lymph nodes, associated medical conditions, external beam radiotherapy {EBRT}, chemotherapy and hormone therapy].

Results

100 patients of early breast cancer between 20 and 65 years were included in the study. 50 patients underwent MRM and 50 underwent WLE&AC. Mean age of the patients was 47.68±8.11 years [in MRM group mean age was 49.38±7.37 years, and in WLE&AC group mean age was 45.98±8.52 years, p value<0.05]. 47[47%] patients were premenopausal and 53[53%] were post menopausal. In the MRM group 17[38%] were pre menopausal and 33[66%] were postmenopausal, in WLE&AC group 30[60%] were pre menopausal and 20[40%] were post menopausal.

99[99%] patients presented with lump breast, 1[1%] had nipple discharge only, 1[1%] had both lump and nipple retraction. 3[3%] patients had pain along with lump. Duration of symptoms at the time of presentation was 3.90±3.55 months in MRM group and 2.5±2.21 months in WLE&AC group [p value<0.05]. Right side was affected in 53[53%] and left side in 47[47%] patients. 59[59%] patients had lump in upper outer quadrant, 23[23%] in UIQ, 13[13%] in LOQ and 5[5%] in LIQ. 15[15%] patients had lump size <2 cm, 45[45%] between >2–3 cm, 34[34%] between >3–4 cm, 6[6%] between >4–5 cm. 39[78%] patients in WLE&AC had lump size <3 cm as compared to 21[42%] in MRM [p value<0.01]. 32[64%] patients in MRM and 20[40%] in WLE&AC group had clinically palpable axillary lymph nodes [p <0.05]. On clinical staging 9[9%] patients were in stage I [1{2%} in MRM and 8{16%} in WLE&AC group], 91[91%] were in stage II [49{98%} patients in MRM and 42{84%} in WLE&AC group].

On histopathological examination 91[91%] patients had infiltrating duct carcinoma, 5[5%] had infiltrating lobular carcinoma, 2[2%] had medullary and 1[1%] had comedo carcinoma. Grade I tumor was seen in 6[6%], grade II in 66[66%], and grade III in 28[28%] patients.

Number of lymph nodes removed in axillary dissection varied from 7 to 32. Average number of lymph nodes dissected were 18. 49[49%] patients had lymph nodes positive for metastasis [in MRM group 30{60%} patients were node positive, in WLE&AC group 19{38%} patients had lymph nodes positive for metastasis p <0.05].

On pathological staging 14[14%] patients were found to be in stage I, of these 3[6%] were of MRM and 11[22%] of WLE&AC group. 40[40%] patients were in stage IIa, of these 18[36%] were of MRM group and 22[44%] were of WLE&AC group. 29[29%] patients were in stage IIb, 21[42%] were in MRM group and 8[16%] in WLE&AC group, 17[17%] patients were in stage III [on clinical examination they were in stage II, hence included in the study].

57[57%] patients were positive for estrogen receptors and 53[53%] were positive for progesterone receptors. 23[48.93%] premenopausal and 34[64.15%] postmenopausal

patients were positive for receptors. Her-2-neu study was done in 67 patients and 13[19.40%] were positive for the same.

89[89%] patients were given chemotherapy [49[98%] in MRM group and 40[80%] in WLE & AC group]. Tamoxifen was given in 57[57%] patients and 4[4%] were put on aromatase inhibitors. 57[57%] were given EBRT [7{14%} in MRM and 50{100%} in WLE&AC group]. Chemotherapy was not given to 8[8%] patients [stage I], it was refused by 3[3%] patients. 1[1%] patient received 3 cycles of neo adjuvant chemotherapy with completion of chemotherapy after surgery. 1 patient of MRM group refused radiotherapy.

In immediate complications, wound sepsis was commonest, seen in 7[7%] patients [4{8%} in MRM and 3{6%} in WLE & AC group]. Seroma was seen in 3[6%] patients and flap necrosis in 1[1%] patients.

Symptoms reported by patients on likert scale on follow up visits were studied. 60 [60%] patients reported one or more symptoms. One symptom was reported by 23[23%] patients, two by 14[14%], three by 15[15%], four by 7[7%] and 1[1%] reported all 5 symptoms.

The most commonly reported symptoms were numbness and pain [39[39%] each]. 19[38%] patients in MRM and 20[40%] in WLE&AC group reported numbness. It was rated as mild by 36% [18{36%} in MRM and 18{36%} in WLE&AC], mild to moderate by 3% [2% in MRM and 4% in WLE & AC]. 21[42%] patients in MRM and 18[36%] WLE & AC group reported pain. Mild pain was complained by 37[37%], [19{38%} in MRM and 18{36%} of WLE & AC group]. Moderate pain was reported by 2% [2{4%} in MRM and 0% in WLE & AC group].

Arm swelling was seen in 25[25%] patients [16{32%} in MRM and 9{18%} in WLE & AC group]. Mild swelling was reported by 23[23%] patients [14{28%} in MRM and {18%} in WLE & AC group]. 2% patients reported moderate swelling [4% in MRM and 0% in WLE & AC group]. 16[16%] patients reported some limitation of movement of the arm [11{22%} in MRM and 5{10%} in WLE & AC]. Out of these 15% reported mild restriction [8{19%} in MRM and 5{10%} in WLE & AC group]. Moderate restriction was complained by 1% [2% in MRM, 0% in WLE & AC group]. 11[11%] patients reported one episode of infection or inflammation in the arm or chest wall or breast [8{16%} in MRM and 3{6%} in WLE & AC group].

There was no statistically significant difference in the reporting of symptoms in the two groups. Patient and treatment factors were analyzed using logistic regression analyses. In the multivariate model numbness was associated with EBRT, associated medical conditions and type of operation [p value<0.01, <0.01, and <0.05 respectively]. Pain had no significant association. Swelling was associat-

ed with EBRT, number of lymph nodes positive for metastases, associated medical conditions, type of operation [p value <0.01, <0.05, <0.05, and <0.01 respectively]. Limited motion had association with number of positive lymph nodes [p value <0.01]. Infection was associated with positive lymph nodes and associated medical conditions [p value <0.05, <0.05 respectively].

Factors that were not significant in predicting complications included age, clinical condition of axilla at presentation, BSA, total lymph nodes removed, chemotherapy, hormone therapy.

Discussion

Near the end of 19th century a variety of surgical techniques were described for the treatment of breast cancer. Moore recommended complete removal of the breast, Gross, excision of the axillary contents when nodes were involved, Volkmann, removal of pectoral fascia and excision of both pectoral muscles in certain cases; Kuster, a systematic clearing out of the axilla and Heidenhan, removal of superficial portion of the pectoralis major muscle and the entire muscle when the cancer is adherent to the chest wall. In 1891 Halstedian mastectomy became the hallmark of “Proper” surgery [19].

Since then it has evolved from radical mastectomy to MRM to quadrantectomy to WLE&AC. Several studies and trials have subsequently proved that breast conservation is an equally effective treatment of breast cancer [20–22].

Treatment of axilla has also changed over time. Fisher et al. were the first to support the hypothesis that axillary dissection has prognostic significance [23]. This led to the use of various options in the management of axilla, including axillary dissection, axillary clearance, axillary dissection with regional lymph node radiation, regional radiation alone, axillary sampling, endoscopic axillary clearance, sentinel lymph node biopsy, and observation [23–29].

Early breast cancer constitutes about 30% of breast cancer cases seen at regional cancer centres in India as compared to 60–70% in the developed world [30]. Median age of the patients in India is 47 years [31]. 73% of the white female patients are post menopausal and only 35%, 49% and 52% of Asians, blacks and mixed race respectively are post menopausal [32]. In this study 53% patients were post menopausal. Lump is the chief complaint in 96.5% and pain in 15.8% [31]. Approximately 40–50% of breast cancers are located in upper outer quadrant, one quarter in juxta areolar area and remainder randomly distributed throughout medial and lower outer quadrant of the breast [33]. In our study also 59% patients had lump in upper outer quadrant.

In a study at AIIMS 16% patients had stage I and 74% had stage II disease [31], whereas in developed countries 50–60% patients present with stage I disease [34–36]. In this study also on pathological staging 14% patients were in stage I, 69% were in stage II and 17% were in stage III.

Breast conservation surgeries constitute 50–75% of operations in early breast cancer in the western world [37, 38]. In India BCS is performed in only 25% of patients of early breast cancer [39]. In our institute 32% of the patients of early breast cancer underwent breast conserving surgery.

In a study by Raina et al. on EBC patients, 53.13% were node negative, 32.61% had 1–3 lymph nodes positive and 14.25% had > 4 lymph nodes positive [31]. In our study 51% patients were node negative, 32% had 1–3 lymph nodes positive and 17% had 4 or more lymph nodes positive for metastasis.

In studies from Europe and America 60–80% patients were receptor positive [40, 41]. Various Indian studies have shown receptor positivity as 43.9%, 50.5% and 53% [31, 42, 43]. In this study also 57% patients were estrogen receptor positive and 53% were positive for progesterone receptor. This may be due to lower average age at diagnosis or real racial differences. Her-2-neu positivity has been found to be between 20 and 30% [44]. In our study it was 19.40%.

There are many options for the management of axilla in early breast cancer. Most women with EBC do not have axillary node metastasis and axillary dissection provides prognostic information without any obvious therapeutic advantage. The largest benefits of ALND were seen in ER-positive women with small primary tumors who might not be candidates for adjuvant chemotherapy if their lymph nodes test negative. Virtually no benefit results in ER-negative women, almost all of whom would receive adjuvant chemotherapy [45].

ALND produces arm problems or psychological distress in about 80% of patients [46]. Previous studies have focused on the adverse effects of lymph node dissection with relatively short term follow up.

In a cohort study, Maunsell et al. [46] interviewed 223 consecutive patients at 3 months and again at 18 months after breast carcinoma surgery. 93% of these patients had undergone an ALND. At 3 months after surgery 82% patients reported at least one arm problem. The variety of problems included swelling [24%], weakness [26%], limitation of arm movement [32%], stiffness [40%], pain [55%] and numbness [58%]. The prevalence of symptoms had not changed significantly at 18 months after surgery. Patients who reported more symptoms were found to have higher levels of psychological distress.

Other studies have used objective measurements to assess morbidity. Lin et al. measured arm size and shoulder

range of motion for 122 patients who had ALND at least 1 year previously [47]. They reported that 39% of patients had more than 15° of restriction of shoulder motion and more than 2 cm of arm swelling. Ivens et al. assessed morbidity by administering a questionnaire to 126 consecutive patients who had undergone full ALND at least 6 months previously. Of these patients 54 had undergone surgery at least 2 years previously. Problems reported by the group included numbness [70%], pain [33%], weakness [25%], swelling [24%] and stiffness [15%].

In no case were the symptoms described as severe, though the symptoms interfered with daily living in 39% of cases. Patients who had undergone surgery more than 2 years previously reported a lower incidence of pain and numbness though the difference was not statistically significant [48].

A cross sectional study was conducted by Marc.A. Warmuth, et al. on 432 stage 1 and 2 breast cancer patients [49]. Patients had undergone surgery 2–5 years previously. Numbness was reported by 35% patients, pain by 30%, arm swelling by 15% and limitation of arm motion by 8%. 8% reported episodes of infection or inflammation at some point since the diagnosis of breast carcinoma.

In a study by Nagel et al. on 106 breast cancer patients, lymphedema was present in 13%, restriction of shoulder function in 24%, while 93% had impaired sensation in axillary region. Lymphedema and restriction in shoulder function were common in patients after adjuvant axillary radiation [3].

In a prospective study, it was found that even 5 years after diagnosis, 38% of patients were still experiencing arm problems (swelling and limited movement). Consistently over the 5 years, quality of life was significantly ($p < 0.001$) lower for patients with arm difficulties. For those whose arm problems dissipated, quality of life significantly improved ($p < 0.01$).

A logistic regression analysis showed that extent of axilla surgery ($p < 0.003$), co morbidity (CVD and diabetes) ($p < 0.003$), employment ($p < 0.01$), younger age ($p < 0.02$), and operating clinic ($p < 0.05$) significantly contributed to arm problems [50].

In our study 60% of the patients reported one or more symptoms. Numbness and pain were the most common symptoms [39% each]. Majority of the patients reported mild to moderate symptoms with only a few saying that they interfered with daily activities.

No major difference in reporting of symptoms was noted in two groups. But it was seen that type of operation was associated with swelling and numbness. EBRT was associated with numbness and swelling and associated medical condition had association with reporting of episodes of infection and swelling. Number of positive lymph nodes were associated with limited motion, infection and swell-

ing. Our study was short term and long term study is needed to know the full extent of complications and their effect on daily activities.

Thus we conclude that mild symptoms of ALND are very common and severe complications very rare. There is no major difference in the reporting of symptoms in WLE&AC and MRM groups. Concerns regarding serious sequelae from ALND should not be a major factor in treatment decision. However SLNB in selected patients may reduce these symptoms even more.

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