

MORBIDITY AND MORTALITY IN BREAST CONSERVATION SURGERY IN EARLY CARCINOMA BREAST

Muhammad Shahbaz Bakht Kayani, Muhammad Zaheer, Naeem Ashraf, Asad Mahmud Malik

Fauji Foundation Hospital, Rawalpindi

ABSTRACT

Objective: To study the mortality and morbidity after breast conservation surgery (BCS) in patients with early breast cancer and comparison with local and international literature.

Design: An Interventional descriptive study.

Place and Duration of study: Fauji Foundation Hospital, Rawalpindi from Jan 2002 to Dec 2003.

Patients and Method: Thirty diagnosed cases of early breast cancer in clinical stage I and II were included. Patients with solitary lump with size up to 4 cm in biggest diameter, 5 cm with large sized breasts and patients with lump in one breast were included. Patients with multicentric diseases, lump larger than 4 cm in size in greatest dimension, lump situated beneath areola, lumps fixed to skin or deeper structures were excluded.

Result: There were 2 (6.67%) cases of seroma formation and 1 (3.33%) case of wound infection, 8 (26.67%) patients suffered persistent painful shoulder movements and arm pain, 4 (13.33%) patients suffered breast disfigurement. 3 (10%) cases of loco-regional recurrence. 1 (3.33%) patient underwent mastectomy and 2 (6.66%) patients underwent further local excision. Percentage of ductal carcinoma in post-menopausal women was also high. There was no mortality.

Conclusion: Breast conservation surgery is equally effective as mastectomy in the treatment of early breast cancer as there is no statistically significant difference in disease-free survival and overall survival.

Keywords: Breast cancer, breast conserving surgery, mortality, morbidity

INTRODUCTION

Breast Cancer is the most common cancer in female population and a leading cause of death in females [1]. Its incidence is high in North European countries, intermediate in South America and low in Africa and Asia [2]. Different studies done in Pakistan have shown breast cancer to be the number one female malignancy. Pakistani women are younger at presentation as compared to their European counter-parts and late stage presentation is also common [3,4]. Breast

cancer also affects male population which accounts less than 2%. In breast cancer patients long-term survival depends not only on the early detection but also on various prognostic markers. In the recent years there has been a trend towards breast conservation surgery followed by radiotherapy to breast and axilla if required. Various procedures for breast conservation include lumpectomy, wide local excision and quadrantectomy. Different trials worldwide have shown no differences in disease-free and overall survival in the patients treated by the Patey's mastectomy or breast conservation surgery. Today, the success of adjuvant chemotherapy and irradiation has greatly altered prospects for therapy the majority of

Correspondence: Dr. Muhammad Shahbaz Bakht Kayani, Assistant Prof of Surgery, Foundation University Medical College, Rawalpindi

Received Nov 25, 2006; Accepted May 8, 2008

patients (80 percent) can at least expect loco-regional control despite systemic metastases.

We conducted the study in our department in 30 patients with stage I and II and noted mortality, postoperative complications and local recurrence in these patients.

PATIENTS AND METHODS

This prospective study was conducted in the department of surgery, Fauji Foundation Hospital Rawalpindi, from January 2002 to December 2003 and their follow-up continued to date. Thirty patients were selected during the above mentioned period, from the patients presenting with breast carcinoma. Patients with early breast cancer in clinical stage I and II with solitary lump, size up to 4 cm in biggest diameter, lump up to 5 cm with large sized breasts to allow adequate wide local excision and lump in one breast were included in the study. Patients with multicentric disease lump larger than 4 cm in size in greatest dimension, lump situated beneath areola and lumps fixed to skin or deeper structures were excluded. Staging was done on the basis of triple assessment i.e.; clinical, radiological (mammography), and tissue diagnosis. Patient data including, age, breast side involved, clinical stage, address, date and details of surgery and immediate postoperative complications and complications during follow-up were recorded in specially designed proforma. Informed written consent regarding nature of surgery, potential side effects like breast disfigurement and local recurrence, was obtained from all patients.

Patients reported for regular follow up as tamoxifen and other investigations are provided free.

Standard operative technique of Wide Local Excision was used i.e., tumor along-with 1 cm of macroscopically normal breast tissue. Axillary sampling was performed aiming to sample at least 4 lymph nodes irrespective of the level. At the end of operation both breast and axillary wounds were drained separately by using suction

drain. Single pre-operative dose of antibiotic was given. Drains were removed after 24 hours if no discharge was present in the drain. Shoulder physiotherapy was started on first postoperative day and skin sutures removed on seventh postoperative day.

Radiotherapy in doses of 5,000 Gy was given to residual breast three weeks after operation. Radiotherapy was given to axilla only if axillary lymph nodes showed metastatic spread by the tumor. Chemotherapy regimen using cyclophosphamide, doxorubicin and fluorouracil was given. All patients received tamoxifen 10 mg b.i.d.

Patients were followed in the out patient department on one monthly interval as Tamoxifen is provided by the hospital on monthly bases. Patients were examined for Lymphoedema, shoulder stiffness, arm pain and disfigurement of the breast. Patients were also examined thoroughly for local recurrence in the breast and axilla. Systemic query was made to rule out systemic metastases and appropriate investigations were done. First post-operative baseline mammogram was done six months after surgery and then yearly, to detect impalpable local recurrence in the residual breast. Patients with local recurrence were evaluated to find distant spread of the disease. All patients reported regularly for follow up.

RESULTS

Age ranges from 34 to 70 years with mean age of 48.8 years (table-1). Out of 30 patients, only 1 (3.33%) patient presented in clinical stage I, all other patients i.e. 29 (96.67%) patients presented in clinical stage II. Twelve (40%) patients had palpable, mobile axillary lymph nodes whereas eighteen patients (53.33%) had no clinical involvement of axillary nodes. 17 (56.67%) patients had left breast whereas 13 (43.33%) patients had right breast involved. Twenty seven (90%) patients had ductal cell carcinoma, one patient (3.33%) had papillary variety, one (3.33%) had medullary and one patient (3.33%) had mucinous carcinoma (fig. 1). Regarding

histological grade (modified Bloom and Richardson System) only one (3.33%) patient had grade I tumor, twenty (66.67%) patients had grade II and nine (30%) patients had grade III tumor (table-2). Out of 30 patients, 5 (16.67%) patients were positive for residual tumor in bed biopsies or cavity shaving. Nineteen (63.33%) patients had histological involvement of axillary lymph nodes whereas 11 (36.67%) patients were free of axillary node metastases (fig. 2). One (3.33%) patient underwent mastectomy as cavity shavings showed invasive component. Other 2 (6.67%) patients were selected for further local excision because bed biopsies showed extensive in situ component. So the rate of re-excision was 10%. Other 2 patients had mild degree of in situ component, so they were not considered for further surgery. Resection margins were clear in patients, treated with further local excision. One (3.33%) patient developed wound infection in axillary wound and seroma formation occurred in two (6.67%) patients. Eight (26.67%) patients complained of persistent pain in ipsilateral arm and scar (table-3). Local recurrence occurred in three (10%) out of 30 patients. One (3.33%) patient had recurrence in axilla where as other Two (6.67%) patients had recurrence in residual breast. There was no mortality.

Table-1: Age Distribution (n=30).

Age (years)	Percentage %
30	0
31 - 40	16.67
41 - 50	43.33
51 - 60	30
61 - 70	10

Table-2: Histological Grade of the Tumor (n=30).

Tumor Grade	No of Patients (%)
I	1 (3.33)
II	20 (66.67)
III	9 (30)

Table-3: Post-operative Complications (n=30).

Complications	No of patients (%)
Seroma	2 (6.67)
Wound Infection	1 (3.33)
Shoulder and Arm Pain	8 (26.67)
Disfigurement	4 (13.33)

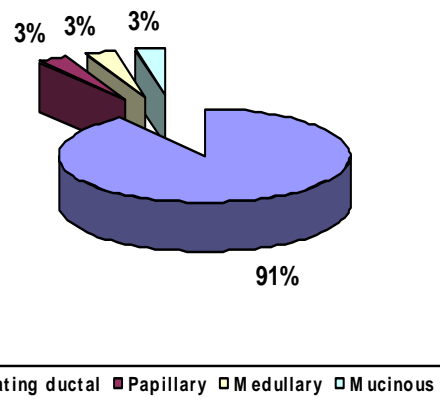


Fig. 1: Pathological types of tumors.

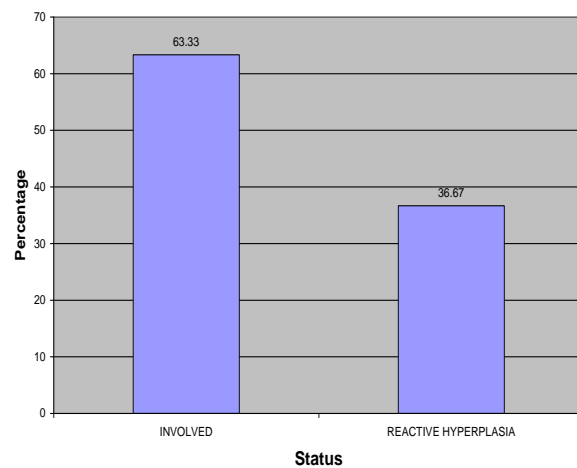


Fig-2: Histological status of axillary lymph nodes (n=30).

DISCUSSION

Breast cancer is the most common cancer in female population and a leading cause of death in females. Its incidence is high in North European countries, intermediate in South America and low in Africa and Asia [1]. The incidence of breast cancer is increasing in developing countries [2,3]. Different studies done in Pakistan have shown breast cancer to be the number one female malignancy. Pakistani women are younger at presentation as compared to their European counter-parts and late stage presentation is also common [4, 5]. Its occurrence is commonest in fourth decade of life [4-6]. Breast cancers also effects male population but among breast cancer patients only less than 2% patients are men. Treatment of locally advance breast tumors (stage III and IV) is mastectomy along with systemic therapy. Loco-regional treatment of

early breast cancer (Stage I and II) is controversial as, it can be treated either by mastectomy or breast conservation. Breast conserving surgery gives good loco-regional control of the disease in addition it gives psychological advantage and increase freedom of dress, to the patient [7]. Overall survival and distant disease-free survival are the same except for local recurrence, which is slightly more common in patients treated with breast conservation.

Different prospective randomized trials have compared mastectomy with conservative surgery and radiation for stage I and II breast cancer. At a follow-up of up to 18 years, none of the trials show significant differences in overall or disease-free survival with either treatment [8-14]. In particular, survival has not been found to improve in patients with histologically positive nodes treated with mastectomy and chemotherapy in either the Milan I trial or the NSABP B-06 trial [10]. The Milan I trial showed a survival benefit that was not statistically significant in axillary node-positive patients treated with quadrantectomy and radiotherapy compared with radical mastectomy.

In different randomized trials, no significant difference was seen in the risk of a recurrence in the treated breast or chest wall after mastectomy. In the National Cancer Institute (NCI) trial, a significantly higher local failure rate was observed in the breast-conservation group [11]. However, in this trial, only gross tumor removal was required for study entry. Local recurrence after breast preservation may be the result of inappropriate patient selection, inadequate surgery or radiation therapy, or biologically aggressive disease. One trial conducted in Japan comparing mastectomy with breast conservation, also concluded that there was no difference in survival for both arms and incidence of local recurrence remained same [15]. Another trial, comparing mastectomy with breast conservation, followed patients for 10 years. There was no difference in overall survival (66% versus 65%) for mastectomy and BCS respectively and

incidence local recurrence was 12% in mastectomy group as compared to BCS, where it's incidence was 20% [16]. Same results were obtained in other studies [17]. Overall, the incidence of recurrence in the treated breast ranges from 3% to 19% [8-11,14]. Most failures in the treated breast can be salvaged with mastectomy, and survival after such treatment is approximately 70% at 5 years. Primary mastectomy does not guarantee freedom from local recurrence in stage I and II breast cancer and the incidence of chest wall recurrence after mastectomy ranges from 4% to 14%. The desire to avoid local recurrence is not a reason to encourage a patient who otherwise is a good candidate for breast conservation to choose mastectomy, because the procedures are associated with an equal risk of local failure.

Nine prospective randomized trials comparing conservative surgery and radiation with mastectomy recently underwent meta-analysis. No survival differences were found in seven of these trials. Local recurrence was reported in 6.2% of the mastectomized patients and 5.9% of the patients treated with breast conservation [18].

The results of multiple nonrandomized retrospective studies further support the equal effectiveness of breast-conservation treatment and mastectomy in appropriately selected patients. At 10 years, overall survival has ranged from 67% to 86%, depending upon the stage of the disease. Disease-free survival at 10 years is approximately 70% [19]. These series have also shown excellent long-term control within the treated breast with primary tumors 5 cm in diameter or smaller. At 10 years, local recurrence rates range from 8% to 19% and for patients with negative margins of resection, the 10-year actuarial risk of breast recurrence is 10% or less [20,21]. The overall survival and local control rates in the breast reported by these retrospective series are comparable to the results of the prospective randomized trials [22,23].

Breast cancer occurrence is commonest in fourth decade of life [4-6]. In our study, maximum number of patients presented

between the ages of 40 to 50 years (43.3%). Median age at presentation was 48.8 years as compared to 48, 45 and 40 years respectively in other studies [4,6,9]. In our study 56.67% patients had left breast involved whereas 43.33% patients had right side involved as compared to Sheikh et al, percentage of breast side involved was 52.38% and 47.62% for left and right sides respectively [24]. In our study, 3.33% patients were in clinical stage I and 96.67% patients in stage II. In our study 36.67% patients were in pre-menopausal age and 63.33% patients were post-menopausal. These findings are different from the findings of study by Rana et al, in which 48% of patients were pre-menopausal and 52% of patients were post-menopausal [6]. Twenty-seven (90%) patients had ductal carcinoma whereas one (3.33%) patient had papillary variety, one (3.33%) patient had medullary and one (3.33%) patient had mucinous carcinoma. Naseer in his study reported the ratio of 93.9% for infiltrating ductal carcinoma, 1.2% for medullary, 1.2% for infiltrating lobular and 1.2% for papillary carcinoma [4]. Various other studies in Pakistan have showed percentage of infiltrating ductal carcinoma being 81.99%, 82.8% and 82.85% [4,8,16]. Infiltrating ductal carcinoma is also the commonest pathological type of breast cancer in USA women [25]. In the present study a marginally high ratio of infiltrating ductal carcinoma was observed. Regarding histological Grade (modified Bloom and Richardson System) only 3.33% patients had Grade I tumor, 66.67% patients had Grade II and 30% patients had Grade III tumors. Shahid et al in his study, found 6.11% cases in Grade I, 65% cases in Grade II and 24% cases in Grade III [22]. Residual tumor or extensive in-situ component (EIC), in the remaining breast, are the indications for further excision or mastectomy. Five (16.67%) patients were positive for residual tumor in the bed biopsies and tumor bed analysis. One (3.33%) patient underwent mastectomy (patient's preference) whereas, two (6.66%) patients were treated with further local excision. So rate of re-operation was about 10%. Studies by Rosen et al and Malik et al

Purushotham et al showed rate of re-excision 2% and 16.4% respectively [25,26]. In the present study, nineteen (63.33%) patients had histological involvement of axillary lymph nodes whereas 11 (36.67%) patients were free of axillary node metastases. The rate of axillary lymph node metastases for state II tumors was 54% in study by Silverstein et al [27].

In our study, one (3.33%) patient developed infection in axillary wound. It was treated with dressings and appropriate antibiotics. Zakezenia et al reported an overall 8.9% wound infection in his study, but in his study all post-operative wounds (other than breast surgeries) were considered which also included contaminated wounds [28]. Seroma formation occurred in (6.67%) patients, which was successfully aspirated. Wood Word et al reported 2.5% to 8.5% rate of Seroma formation [29]. About 26.67% patients complained of persistent pain in ipsilateral arm and scar pain. In another study the incidence of arm & scar pain was 25 - 30% [30]. Local recurrence occurred in three (10%) out of 30 patients, one (3.33%) patient had recurrence in axilla and, two (6.66%) patients had recurrence in breast. Different randomized trials by Arriagada R et al, Blichert-Toft et al, Fowble, and Kurtz et al, have shown local recurrence rates of 3% to 19% [8,9,31]. Local recurrence of 4 to 14% are reported after Patey's mastectomy [16].

The patient who developed recurrence in the axilla had not received axillary irradiation, as there was no histological involvement of axillary lymph nodes. None of the recurrences occurred in patients who were re-operated for positive resection margins.

In the present study age distribution pattern was almost same with other local studies. Invasive ductal carcinoma occurred in 90% of the cases, which is a slightly higher percentage as compared with other studies, in which this percentage was 81.99%, 82.8% and 85.85%. Naseer in his study found percentage of invasive ductal carcinomas of 93.99% [4]. This percentage is higher as compared to European counter-parts. There was no

difference in complication rate when compared with other studies. Post-menopausal women were more as compared to pre-menopausal women. Rate of re-operation was 10.34%, which is slightly higher than mentioned in other studies. Local recurrence rate was 10.33%. This is comparable with local recurrence rate in other studies.

CONCLUSION

Breast cancer is the most common female malignancy in the whole world and Pakistan as well. Breast conservation surgery is an effective way of treatment for early breast cancer patients. It provides good loco-regional control of the disease along with excellent information for staging of the disease. In addition it provides psychological advantage to the patient and prevents undue axillary surgery in node-negative patients. Local recurrence is marginally more common in breast conservation surgery but overall survival and distant disease-free survival are the same if compared with Patey's mastectomy. So it is an effective mode of treatment and patients presenting in early breast cancer, should be considered for breast conservation surgery.

REFERENCES

1. Kelsey JL, Horn-Ross PL. Breast cancer: magnitude of the problem and descriptive epidemiology. *Epidemiol Rev.* 1993;15:6-17
2. Parkin DM. Cancer in developing countries. *Cancer Surv.* 1994; 19-20: 519-61
3. Abdullah P, Mubarik A, Zahir N, Rehman ZU, Sattar A, Mehmood A. Breast lumps: what they actually represent. *J Coll Physicians Surg Pak.* 1998; 9; 1: 46-8.
4. Ahmad N. Breast carcinoma in Pakistani women: how it differs from the west. *J Surg.* 1991; 2: 56-8.
5. Rashid M, Rafi CM, Mamoon N. Late presentation of carcinoma breast in Pakistani women. *Pak Armed Forces Med J.* 1996; 46(2):11-5.
6. Rana F, Younis J, Muzammil A, Raza S, Khawar S, Khan U, et al. Breast cancer epidemiology in Pakistani women. *J College Physicians Surg Pak.* 1999; 8(1): 20-3
7. Ghazal SK, Fallowfield L, Blamey RW. Comparison of psychological aspects and patient satisfaction following breast conserving surgery, simple mastectomy and breast reconstruction. *Eur J Cancer.* 2000 Oct 01; 36; 15: 1938-43.
8. Arriagada R, Le MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: Patterns of failure with 15 years of follow-up data. *Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol.* 1996; 14(5): 1558-64.
9. Blichert-Toft M, Rose C, Andersen JA, Overgaard M, Axelsson CK, Anderson KW. Danish randomized trial comparing breast conservation therapy with mastectomy: Six years of life-table analysis. *J Natl Cancer Inst Monogr.* 1992; (11): 19-25.
10. Veronesi U, Luini A, Galimberti V, Zurrida S. Conservation approaches for the management of stage I/II carcinoma of the breast: Milan Cancer Institute Trials. *World J Surg* 1994; 18: 70-5.
11. Jacobson JA, Danforth DN, Cowan KH, Td'Angelo SM, Steinberg SM, Pierce L. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med.* 1995; 332: 907-11.
12. Van Dongen JA, Bartelink H, Fentiman IS, Lerut T, Mignolet F, Otthuis G et al. Factors influencing local relapse and survival and results of salvage treatment after breast-conserving therapy in operable breast cancer: EORTC trial 10801, breast conservation compared with mastectomy in TNM stage I and II breast cancer. *Eur J Cancer.* 1992; 28A(4-5): 801-5.
13. Liljegren G, Holmberg L, Adami HO, Westman G, Graffman S, Bergh J, et al. Sector resection with or without postoperative radiotherapy for stage I breast cancer: five-year results of a randomized trial. *J Natl Cancer Inst.* 1994; 86(9): 717-22.

14. Van Dongen JA, Bartelink H, Fentiman IS, Lerut T, Mignolet F, Olthuis G, et al. Randomized clinical trial to assess the value of breast-conserving therapy in stage I and II breast cancer: EORTC 10801 trial. *J Natl Cancer Inst Monogr.* 1992; (11): 15-8.
15. Noguchi M, Yagasaki R, Kawahara F, Minami M, Tsuyama H, Earashi M, et al. Breast conserving treatment versus modified radical mastectomy in Japanese patients with operable breast cancer. *Int Surg.* 1997; 82 (3): 289-94.
16. Van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: european organization for research and treatment of cancer 10801 trial. *J Natl Cancer Inst.* 2000 Jul 19; 92(14): 1143-50.
17. Horiguchi J, Iino Y, Takei H, Sugamata N, Maemura M, Yokoe T. Comparison of breast-conserving therapy with mastectomy for treatment of early breast cancer. *Anticancer Res.* 1997;17;5B:3849-55.
18. Effects of radiotherapy and surgery in early breast cancer: an overview of the randomized trials. Early Breast Cancer Trialists' Collaborative Group. *N Engl J Med.* 1995; 333: 1444-55.
19. Dewar JA, Arriagada R, Benhamou S, Benhamou E, Brelel JJ, Pellae-Cosset B, et al. Local relapse and contralateral tumor rates in patients with breast cancer treated with conservative surgery and radiotherapy (Institut Gustave-Roussy 1970-1982). *Cancer.* 1995; 76(11): 2260-5.
20. Fisher B, Anderson S, Redmond CK, Walmark N, Wickerham DL, Cronin WM, et al. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med.* 1995; 333: 1456-61.
21. Mansfield CM, Komarnicky LT, Schwartz GF, Rosenberg AL, Krishman L, Jewell WR, et al. Ten-year results in 1070 patients with stages I and II breast cancer treated by conservative surgery and radiation therapy. *Cancer.* 1995; 75(9): 2328-36.
22. Shahid Siddiqui M, Kayani M, Sulaiman S, Akbar S, Sajid H, Muzaffar S. A Morphological Study of 572 Breast Specimens. *J Pak Med Assoc.* 2000; 50 (6): 173-7.
23. Shaikh SA, Burdi GM, Shaikh SM. Cancer breast: Larkana experience. *Pak J Surg.* 1994; 10: 88-92
24. Rosen PP, Kinne DW. Breast carcinoma in women 35 years of age or younger. *Am J Clin Pathol.* 1984; 81: 804.
25. Malik HZ, Purushotham AD, Mallon EA, George WD. Influence of tumour bed assessment on local recurrence following breast-conserving surgery for breast cancer. *Eur J Surg Oncol.* 1999;25(3): 265-8.
26. Silverstein MJ, Gierson ED, Waisman JR, Senosfsky GM, Golburn WJ, Gamagani P. Axillary lymph node dissection for T1a breast carcinoma. *Cancer.* 1994; 73: 664-7.
27. Anielski R, Barczynski M. [Postoperative wound infections. I. Population data and risk factor] [Article in Polish]. *Przegl Lek.* 1998; 55 (3): 101-8.
28. Woodworth PA, McBoyle MF, Helmer SD, Beamer RL. Seroma formation after breast cancer surgery: incidence and predicting factors. *Am Surg.* 2000; 66 (5): 444-50; discussion 450-1
29. Tasmuth T, Von Smith K, Kalso E. Pain and other symptoms during the first year after radical and conservative surgery for breast cancer. *Br J Cancer.* 1996; 74 (12): 2024-31.
30. Fowble B. Ipsilateral breast tumor recurrence following breast-conserving surgery for early-stage invasive cancer. *Acta Oncol.* 1999; 38(Suppl 13): 9-17.
31. Kurtz JM, Amalric R, Brandone H, Ayme Y, Jacquemier J, Pietra JC, et al: Local recurrence after breast conserving-surgery and radiotherapy: Frequency, time course, and prognosis. *Cancer.* 1989; 63: 1912-17.