Results of breast conserving surgery in clinical stage I-II breast carcinoma

Erhan Erdem · Haluk Alagol

Received: 15 May 2008 / Accepted: 18 October 2008
© Association of Surgeons of India 2009

Abstract

Background The role of breast conserving surgery with radiotherapy is well established and has become a widely used procedure in breast cancer. Patient selection, a multidisciplinary approach, and expert surgical technique are important factors to avoid locoregional recurrence. The aim of this study was to analyse the outcomes of patients treated with breast conserving surgery in stage I-II breast cancer.

Methods In this study, the results of 135 breast conserving surgery cases are reported. The majority of patients received radiotherapy and adjuvant systemic treatment.

Results At a median follow-up period of 54 months, 5 patients (3.7%) developed locoregional recurrence. The 5 years overall and disease-free survival rates were 90% and 84%, respectively. Young age, lymph node involvement, and oestrogen receptor negativity were independent predictors for overall survival.

Conclusion In selected patients, breast conserving surgery using good surgical technique in conjunction with radiotherapy can achieve a high survival rate with a low locoregional recurrence rate.

Keywords Breast carcinoma · Breast conserving surgery

Introduction

Breast conserving surgery (BCS) has become an alternative surgical procedure used primarily for early stage breast cancer. In the early 1980s, the maximum acceptable tumour size for BCS was 2 cm, and the BCS procedure consisted of a quadrantectomy. In addition, it was generally accepted that BCS was not appropriate for patients with clinically positive lymph nodes. However with advances in radiotherapy and surgical techniques, such as lumpectomy and local excision, BCS can now be performed for larger tumours with more acceptable cosmetic results; lymph node status is no longer considered a contraindication for BCS, since an axillary dissection is performed with an extra incision in nearly all patients. Currently, the most important criterion for BCS is the tumour/breast ratio.

In department of surgery of Ankara Oncology Training and Research Hospital, BCS has been used since 1995 as an alternative to modified radical mastectomy (MRM) in appropriate, selected patients. The aim of this study was to analyse the outcomes of patients treated with BCS in clinical stage I-II breast cancer.

Patients and methods

In this retrospective study breast cancer patients who underwent BCS between February 1995 and December 2005 were enrolled. During this period 144 BCS procedures were performed in 141 patients (3 patients had bilateral malignancies) out of a total of 511 cases with clinical stage I and II breast carcinoma. During the study period it was our department policy to do BCS in patients with T1 and T2 tumours depending on the tumour/breast ratio. BCS was not carried out in multicentric tumours. Re-excision was routine when the margins are very close or positive, and, if sufficient margins cannot be achieved, then a simple mastectomy was performed. Of the 144, 14 required

E. Erdem · H. Alagol
Department of 5th General Surgery,
Ankara Oncology Training and Research hospital
13th Street, Demetevler,
Ankara, Turkey

E. Erdem (✉)
E-mail: er2dem@gmail.com

re-excision because of positive or close margins; 5 of these achieved negative margins, while the other 9 underwent simple mastectomy. Therefore, a total of 135 breast carcinoma cases treated with BCS were followed until April 2008. The BCS consisted of a lumpectomy, a wide excision, or a quadrantectomy combined with level-III axillary lymph node clearance and external beam radiation therapy. Surgical margins <1 mm were considered to be positive and <3 mm were considered to be close margins according to the results of pathological examination. Extent of surgical margins, intraoperative frozen/imprint cytology was used if only there was a doubt about adequacy of margins in time of surgery; instead in routine procedure paraffin wax results were waited. Level-III axillary dissections were performed in all but 9 patients (93.3%) (1 had severe cardiac failure, 4 were very old patients who could not tolerate general anaesthesia, and 4 had in situ carcinoma with microcalcification on mammography and were treated with stereotactic wide excision). Although these 9 patients had no palpable axillary lymph nodes, they were considered as NX. All but 8 (1 patient had LCIS in which radiotherapy was not indicated, 7 patients with cardiac problems in which radiotherapy was contraindicated that 5 of them also could not get general anaesthesia and were not performed axillary dissection as well) of the patients (94%) were treated with radiotherapy to the breast at a dose of 50 Gy. plus a boost of 5–10 Gy; in 2–3 months after surgery. Thirteen of them (9.6%) also received radiotherapy to the axillary region due to the presence of N2 or N3 axillary stages. Adjuvant systemic chemotherapy was given to 96 patients (71%) that had axillary lymph node involvement or were considered to be at high risk for metastasis; adjuvant hormone therapy was given to 90 patients (66.6%) based on their receptor status. Adjuvant therapy has been performed based on the recommendation of the St. Gallen International Conference with the treatment of anthracycline-based regimens (4–6 cycles of CAF or CEF therapy: 600 mg/m² of cyclophosphamide, 60 mg/m² of adriamycin or 60–75 mg/m² of epirubicin and 600 mg/m² of 5-fluorouracil), only 4 patients before 1996 were given 6 cycles of CMF: 600 mg/m² of cyclophosphamide, 40 mg/m² of methotrexate and 600 mg/m² of 5-fluorouracil. In adjuvant hormone therapy, tamoxifene 20 mg/day has been used for 5 years. Recently aromatase inhibitors have also been used in postmenopausal patients, in terms of prolonged or switched therapy. Information was collected concerning age, menopausal status, surgical margins, tumour size, lymph node involvement, hormone receptors, tumour differentiation, p53 status and HER-2/neu status. P53 estimation was done routinely between 2001–2004 years, but it was not in practice earlier.

After completing radiotherapy and chemotherapy, the patients were followed clinically in every 3 months for the first 2 years, then every 6 months for the next 3 years and yearly thereafter. Radiological examinations were also performed in every 6–12 months.

The statistical analysis included Kaplan-Meier survival analysis for disease-free (DFS) and overall survivals (OS), and Cox regression analyses to assess each prognostic factor separately using SPSS 10.0 for windows. A $p < 0.05$ was accepted as significant.

Results

Of the 511 stage I–II breast carcinoma patients, 135 BCS procedures were performed in 132 patients (26.4%) (3 had bilateral carcinoma). The cosmetic results are all good or at least in acceptable condition. The histopathological diagnoses were: invasive ductal carcinoma in 100; lobular carcinoma in 5; mixed lobular + invasive ductal carcinoma in 2; medullary carcinoma in 4; mucinous carcinoma in 5; tubular carcinoma in 3; papillary carcinoma in 2; columnar carcinoma in 1; lobular carcinoma in situ in 1; and ductal carcinoma in situ in 12. The median age at the time of surgery was 49.52 (range, 22–89) years, and the median follow-up was 54 (range, 15–120) months. The patients' characteristics are listed in Table 1. On histopathology, more than 4 positive axillary lymph nodes were found in 6 cases (N2), and a positive infraclavicular lymph node was found in 3 cases (N3). During follow-up, 5 patients (3.7%) developed locoregional recurrence (LR), and 15 patients experienced a distant metastasis (one of these also had a LR). The 5-year DFS and OS rates were 84% and 90%, respectively (Figs. 1 a, b, c). No significant predictive factor for LR could be found. While young age, axillary lymph node metastasis, and ER negative status were positive predictive factors for OS, axillary lymph node metastasis and ER negative status were positive predictive factors for DFS (Table 2).

Discussion

BCS has become the standard treatment for early breast cancer. In various reports, the rate of performing BCS in early breast cancer varies from 10–45% [1, 2]. In our study, the BCS performing rate was 26.4% and this rate has a trend to increase over time, as it was approximately 16.5% before 2000 and 34% after 2000.

BCS was first performed in the 1980s, but the LR rates were rather high (30–40%) [3, 4]. However, the standard use of radiotherapy after BCS has decreased the LR rates to $< 10\%$ [5–9]. Initially, only T1 tumours were selected for BCS, and the acceptable BCS procedure was quadrantectomy, which was defined as the excision of the whole quadrant of the breast tissue in which the tumour was found. Later, with increased technical expertise and a multidisciplinary approach, larger tumours began to be treated more conservatively, with lumpectomy and wide excision of the tumour, so that more cosmetic results could be achieved with similar DFS and LR rates [10]. The two most contro-

Table 1 Characteristics of patients who had BCS

Age	
<40	41
>40	94
Breast conserving surgery	
Lumpectomy	87
Tumourectomy	10
Quadrantectomy	38
Axillary dissection	126
Tumour size	
Tis	9
T1	36
T2	86
T3	4
Lymph node status	
N0	73
N1	44
N2	6
N3	3
NX	9
Grade	
Low	39
High	80
Unknown	16
ER / PR status	
– / –	30
– / +	14
+ / –	22
+ / +	61
Unknown	8
p53	
–	37
+	33
Unknown	65
HER-2/neu	
–	57
+	24
Unknown	54

(BCS, breast conserving surgery; ER, oestrogen receptor; PR, progesterone receptor)

versal issues related to BCS are, whether BCS can achieve the same survival rates as in MRM; and whether LR rates are higher in BCS than those in MRM. In many studies, it is obvious that the mortality rate in BCS is not different from that of MRM, but LR rates appear to be different [11, 12]. In an analysis of the major randomised trials that compared MRM with BCS, all trials showed no difference in the

Fig. 1a Overall survival curve after BCS **Fig. 1b** Disease-free survival curve after BCS **Fig. 1c** Locoregional recurrence free survival curve after BCS

mortality rates with a median follow-up of approximately 14 years, but there were significant differences in LR in some of them. In the National Surgical Adjuvant Breast and

Table 2 Univariate analysis of risk factors for overall and disease-free survivals in BCS

	5-year OS (%)	<i>p</i> value	5-year DFS (%)	<i>p</i> value
Age				
<40	79		75	
>40	97	0.003	93	NS
Tumor status				
<2 cm	92		86	
>2 cm	93	NS	85	NS
Axillary nodal status				
N-	97		95	
N+	83	0.019	72	0.015
Grade				
Low	97		82	
High	87	NS	82	NS
ER status				
ER+	97		95	
ER -	77	0.014	58	0.003
PR status				
PR+	96		82	
PR -	85	NS	81	NS
Her-2/neu status				
+	83		72	
-	96	NS	84	NS
p53 status				
+	85		68	
-	97	NS	90	NS

(BCS, breast conserving surgery; OS, overall survival; DFS, disease-free survival; ER, oestrogen receptor; PR, progesterone receptor; NS, not significant)

Bowel Project (NSABP)-06 trials, the LR rate was 14.3% in the BCS arm [4]. In this trial, the LR rate was increased to 39.2% in patients who did not receive radiotherapy. In the European Organisation for the Research and Treatment of Cancer (EORTC) trial, LR was 20% in the BCS arm and 12% in the MRM arm in 10-year follow-up time [13]. Similarly, in the National Cancer Institute (NCI) trial, LR in 18-year follow-up period was 22% [14]. In the Milan trial, LR in 20-year follow-up period was 8.5% in the BCS arm and 2.8% in the MRM arm, but, in this study, only T1 tumours were randomised, and the BCS procedure was quadrantectomy in all patients [15]. In contrast to these four trials, in the Danish and U.S. National Cancer Institute and Gustave-Roussy Institute trials, recurrence-free, disease-free and overall survivals were not significantly different between the BCS and MRM arms [16, 17]. Currently in our clinic, the standard BCS method is a lumpectomy, though quadrantectomy was used initially. As seen in Table 1, most cases had T2 tumours, 97 of the 135 cases had lumpectomy or tumourectomy, and the LR rate was 3.7%, which is

among the lowest rates reported in the literature. The lowest LR rate is reported from India with 1% [18]. The reason of this may be the extent of surgical margins that in their study wide excision with a 1.5 cm three-dimensional gross tumour-free margin had been achieved whereas in many centres 0.5–1 cm margins were accepted as adequate.

Based on a review of the literature, young age, lymph node involvement, negative ER status, high grade, and the presence of an extensive intraductal component were the factors identified as predictive or prognostic factors for OS or DFS, as well as for LR. The most commonly reported factors are young age and lymph node involvement and these factors were also identified in the present study. Several authors reported that in young patients with more aggressive histopathology, the tumours were associated with overexpression of HER-2/neu, a higher incidence of oestrogen and progesterone receptor negativity, and a high nuclear grade; the combination of these unfavourable features is associated with a higher risk of LR or distant recurrence [5–7, 9, 19–22]. Lymph node involvement has also been reported as

another important predictive factor of both survival and LR; it is not surprising that lymph node involvement is mostly associated with aggressive histopathology [5, 8, 23]. However, there have been some reports that lymph node involvement is not a predictive factor for LR [6, 19]. In our study with univariate analysis, young age, lymph node involvement and ER negativity were found to be predictive factors for OS; ER negativity and lymph node involvement were predictive factors for DFS. However, none of these factors were found to be predictive for LR. Although a multivariate analysis would be desirable, we did not perform that because of the limited numbers of end-point events.

Other risk factors for LR have been reported, including nonuse of radiotherapy after BCS, positive or close resection margins and tumour multicentricity [19, 24–27]. However, in the present study, these factors were not assessed because radiotherapy was given to all but 8 patients (7 were very old patients with cardiac problems in which radiotherapy was contraindicated; one had LCIS, for which radiotherapy was not indicated). In addition all of our cases were carefully selected for BCS, keeping the following in mind (which we continue to use as our BCS selection criteria): BCS is primarily performed for T1 and T2 cases, depending on the tumour/breast ratio; all patients are assessed by a multidisciplinary team before surgery, including radiation oncology for adjuvant radiotherapy; BCS is not carried out in multicentric tumours; re-excision is routine when the margins are very close or positive, and, if sufficient margins cannot be achieved, then a simple mastectomy is performed.

One of the important end points of breast conservation surgery is cosmetic outcome and quality of life issues. As our cosmetic results are all in acceptable condition, we did not undertake detailed study on these issues for two reasons. Firstly, as we applied BCS only in a select cohort of our patients we feared that it may introduce selection bias in the analysis of cosmetic outcome. Secondly, our aim was to study LR and survival analysis rather than cosmesis and quality of life analysis.

Based on our results, it would appear that with careful attention to both patient selection and surgical technique, BCS can be performed safely with a lower LR rate, particularly in T1-T2 breast carcinoma cases, independent of any predictive factors.

Conflict of interest The authors do not have any disclosable interest

References

1. Newman LA, Kuerer HM (2005) Advances in breast conservation therapy. *J Clin Oncol* 23:1685–1697
2. Woon YY, Chan MYP (2005) Breast conservation surgery—the surgeon's factor. *Breast* 14:131–135
3. Newman LA, Washington TA (2003) New trends in breast conservation therapy. *Surg Clin N Am* 23:841–843
4. Fisher B, Anderson S, Bryant J, et al. (2002) Twenty year follow-up of a randomized trial comparing total mastectomy, lumpectomy, lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 347:1233–1241
5. Noh WC, Paik NS, Kim MS, Yang KM, Cho CK, Choi DW, et al. (2005) Ipsilateral breast tumor recurrence after breast-conserving therapy: A comparison of quadrantectomy versus lumpectomy at a single institution. *World J Surg* 29:1001–1006
6. Pendlebury SC, Ivanov O, Renwick S, Stevens GN (2003) Long term review of a breast conservation series and patterns of care over 18 years. *Aust N Z J Surg* 73:577–583
7. Borg MF (2004) Breast-conserving therapy in young women with invasive carcinoma of the breast. *Aus Radiol* 48:376–382
8. Malmstrom P, Holmberg L, Anderson H, Mattsson J, Jönsson PE, Tennvall-Nittby L, et al. (2003) Breast conservation surgery, with and without radiotherapy, in women with lymph node-negative breast cancer: a randomized clinical trial in a population with access to public mammography screening. *Eur J Cancer* 39:1690–1697
9. Ohsumi S, Takashima S, Saeki T, Aogi K (2002) Breast-conserving therapy consisting of wide excision, axillary dissection, and radiotherapy for early-stage breast cancer: the experience of the National Shikoku Cancer Center. *Biomed Pharm* 56:196–200
10. Benda R, Mendenhall NP, Lind DS, Cendan JC, Shea BF, Richardson LC, et al. (2004) Breast-conserving therapy (BCT) for early-stage breast cancer. *J Surg Oncol* 85:14–27
11. McCready D, Holloway C, Shelley W, Down N, Robinson P, Sinclair S, et al. (2005) Surgical management of early stage invasive breast cancer: a practice guideline. *Can J Surg* 48:185–194
12. Jatoi I, Proschan MA (2005) Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer. *Am J Clin Oncol* 3:289–294
13. van Dongen JA, Voogd AC, Fentiman IS, Margoless RG, Deutsch M, Fisher ER, et al. (2000) 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* 92:1143–1150
14. Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewehr DJ, et al. (2003) Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy. *Cancer* 98:697–702
15. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. (2002) Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 347:1227–1232
16. Blichert-Toft M, Rose C, Andersen JA, Overgaard M, Axelsen CK, Andersen KW, et al. (1992) Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. *J Natl Cancer Inst Monogr* 11:19–25
17. Arriagada R, Le MG, Guinebreteiere JM, Dunant A, Rochard F, Tursz T (2003) Late local recurrences in a randomized trial comparing conservative treatment with total mastectomy in early breast cancer patients. *Ann Oncol* 14:1617–1622

18. Deo SVS, Samaiya A, Shukla NK, Mohanti BK, Raina V, Purkayastha J, et al. (2005) Breast conservation therapy for breast cancer: Patient profile and treatment outcome at a tertiary care cancer centre. *Nat Med J India* 18:178–181
19. Fredriksson I, Liljegren G, Palm-Sjövall M, Arnesson LG, Emdin SO, Fornander T, et al. (2003) Risk factors for local recurrence after breast-conserving surgery. *Brit J Surg* 90: 1093–1102
20. Yildirim E, Dalgic T, Berberoglu U (2000) Prognostic significance of young age in breast cancer. *J Surg Oncol* 74: 267–272
21. Komoike Y, Motomura K, Inaji H, Kasugai T, Koyama H (2003) Repeat lumpectomy for patients with ipsilateral breast tumor recurrence after breast-conserving surgery. *Oncology* 64:1–6
22. Tartter PI, Kaplan J, Bleiweiss I, Gajdos C, Kong A, Ahmed S, Zapetti D (2000) Lumpectomy margins, reexcision, and local recurrence of breast cancer. *Am J Surg* 179:81–85
23. Vitucci C, Tirelli C, Graziano F, Santoro E (2000) Results of conservative surgery for limited-sized infiltrating breast cancer: analysis of 962 tested patients: 24 years of experience. *J Surg Oncol* 74:108–115
24. Du X, Freeman JL, Nattinger AB, Goodwin JS (2002) Survival of women after breast conserving surgery for early stage breast cancer. *Breast Cancer Res Treat* 72:23–31
25. Huston TL, Simmons RM (2005) Locally recurrent breast cancer after conservation therapy. *Am J Surg* 189: 229–235
26. de Roos MAJ, de Bock GH, Baas PC, de Munck L, Wiggers T, de Vries J (2005) Compliance with guidelines is related to better local recurrence-free in ductal carcinoma insitu. *Br J Cancer* 93:1122–1127
27. Landheer MLEA, Klinkenbijl JHG, Pasker-de Jong PCM, Wobbes Th (2004) Residual disease after excision of non-palpable breast tumors: analysis of tumor characteristics. *Eur J Surg Oncol* 30:824–828