Locoregional Recurrence and Survival Rates after Breast-Conserving Surgery and Hormonal Therapy in 70-Year-Old or Older Patients with Stage I or IIA Breast Carcinoma

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Keywords

Elderly · Early stage breast cancer · Treatment

Summary

Background: Data for treatment of elderly women (≥ 70 years) with estrogen receptor-positive early stage breast cancer are available. We have compared different treatment options to determine whether lumpectomy (LU) plus adjuvant hormonal therapy (HT) is as effective as combined LU, HT, and radiotherapy (RT). **Method:** Medical records of elderly patients over 69 years of age who had been treated for T1N0M0 (stage I) and T2N0M0 (stage IIA) at 2 different medical centers between March 2004 and January 2011 were assessed, and 35 patients were included in this study. 21 of these patients underwent only breast-conserving surgery (BCS) and HT (Group 1: T1N0M0-Group 1a, $n = 16$; T2N0M0-Group 1b, $n = 5$) and the others either BCS, HT and RT (Group 2, $n = 4$) or BCS, chemotherapy (CT), HT and RT (Group 3, $n = 10$). Adjuvant HT for all the patients comprised aromatase inhibitors. **Results:** The mean follow-up period for Groups 1, 2 and 3 were 32.2, 31.3 and 20.4 months, respectively. No locoregional recurrence or cancer-specific mortality occurred in any of these patients; 1 patient from Group 1 died of a different cause. **Discussion:** The BCS+HT regimen seems to be an efficient treatment option for early stage breast cancer in selected 70-year-old and older patient groups.

Schlüsselwörter

Ältere Patientinnen · Mammakarzinom, primäres · Behandlung

Zusammenfassung

Hintergrund: Daten zur Behandlung von älteren Patientinnen (≥ 70 Jahre) mit Östrogenrezeptor-positivem Mammakarzinom im Frühstadium sind verfügbar. Wir haben verschiedene Behandlungsoptionen verglichen, um herauszufinden, ob Lumpektomie (LU) mit adjuvanter Hormontherapie (HT) ebenso effektiv ist wie LU und HT kombiniert mit Radiotherapie (RT). **Methode:** Die Patientenakten von Patientinnen > 69 Jahren, die zwischen März 2004 und Januar 2011 an zwei verschiedenen Zentren wegen eines Mammakarzinoms (T1N0M0 (Stadium I) oder T2N0M0 (Stadium IIA)) behandelt wurden, wurden untersucht und 35 Patientinnen wurden in diese Studie eingeschlossen. 21 dieser Patientinnen erhielten nur eine brusterhaltende Therapie (BCS) und HT (Gruppe 1: T1N0M0; Gruppe 1a, $n = 16$; T2N0M0; Gruppe 1b, $n = 5$). Die anderen Patientinnen erhielten entweder BCS, HT und RT (Group 2, $n = 4$) oder BCS, Chemotherapie (CT), HT und RT (Group 3, $n = 10$). Die adjuvante HT aller Patientinnen enthielt Aromataseinhibitoren. **Ergebnisse:** Das mittlere Follow-up für die Gruppen 1, 2 und 3 betrug 32,2, 31,3 und 20,4 Monate. Keine dieser Patientinnen erlitt ein lokoregionales Rezidiv oder verstarb an Brustkrebs; eine Patientin aus Gruppe 1 verstarb aus anderen Gründen. **Diskussion:** Das BCS+HT-Regime scheint eine effiziente Behandlungsoption für ausgewählte Patientinnen über 69 Jahren mit Mammakarzinom im Frühstadium zu sein.

Introduction

Risk of breast cancer is directly correlated with age. Because incidence and mortality rates increase with ageing, breast cancer is one of the major medical problems in countries with an older population [1]. Of women diagnosed with breast cancer, 40% are aged 65 and older. More women of ≥ 65 years die of breast cancer compared to other cancers [2]. Since overall life expectancy is increasing due to improvements in medicine, in the next decade, a 30% increase in the number of breast cancer cases in the elderly is expected [3]. Generally, elderly patients are excluded from breast cancer studies and also receive less aggressive treatment because of additional health problems [4, 5]. Therefore, for this age group, clinical data are scarce and there is no consensus on treatment modalities. Considering prospective randomized study results showing local recurrence rates of 8% and 1.2% after a 15- and 5.6-year-median follow-up period, respectively, for a tamoxifen (TMX)-only-treated elderly group, it would appear that no adjuvant radiotherapy (RT) is required in patients > 69 years who have small tumors if surgical borders are clean and hormone expressions are positive [6, 7]. However, for such patients aromatase inhibitors (AIs) are thought to achieve better local control than TMX. In the currently running ESTEEM study, estrogen receptor (ER)-positive patients older than 74 years who had operable tumors were randomized into 2 groups receiving: (1) adjuvant anastrozole treatment after standard surgery, or (2) primer anastrozole

treatment without surgery. When the results of this study are published, the outcome of primer hormonal therapy (HT) treatment in the elderly will be much clearer [8]. In our study we assessed the efficiency of a breast-conserving surgery (BCS) plus HT treatment protocol in this age group.

Material and Methods

Data for ≥ 70 -year-old T1N0M0 (stage I) and T2N0M0 (stage IIA) breast cancer patients were assessed at 2 centers between March 2004 and January 2011, and 35 of these patients were included in this descriptive case series study (table 1). All the study patients had undergone BCS and sentinel lymph node biopsy (SLNB). Inclusion criteria were hormone receptor (HR) positivity, clean surgical borders and SLNB negativity. There were 3 treatment options: (1) BCS + HT only (Group 1 comprising T1N0M0-Group 1a (n = 16) and T2N0M0-Group 1b (n = 5)); (2) BCS + HT + RT (Group 2, n = 4), and (3) BCS+ chemotherapy (CT) + HT + RT (Group 3, n = 10). AIs were used as HT in all 35 cases. Mean age, mean tumor size, stage at diagnosis, tumor grade, adjuvant therapy procedures, local relapse during follow-up and mortality rates were assessed.

The study was reviewed by the medical ethics committee and was performed in accordance with the medical ethics standards laid down in an appropriate version of the 1964 Declaration of Helsinki. The study was approved by The Institute's Protocol Review Board.

Results

Between March 2004 and January 2011, 522 patients underwent surgery for breast cancer at these 2 study centers. Of these, 35 (6.7%) were ≥ 70 years. Mean age was 74.5 years (range 70–83). Mean tumor size was 1.9 cm. At diagnosis, 24 patients (68.6%) were considered stage I, and 11 patients (31.4%) stage IIA. 15 patients (42.8%) had grade 1, 16 patients (45.7%) grade 2 and 4 patients (11.4%) grade 3 tumors. BCS + HT was given to 21 patients (60%) (Group 1: T1N0M0-Group 1a, n = 16; T2N0M0-Group 1b, n = 5). Group 2 (n = 4) received BCS + HT + RT, and Group 3 (n = 10) BCS + CT + HT + RT. Mean follow-up period for Groups 1, 2 and 3 were 32.2, 31.3 and 20.4 months, respectively. None of the patients showed locoregional recurrence or breast cancer-specific mortality during follow-up. One patient from Group 1a died of a non-breast cancer-related cause.

Discussion

Aging remains one of the most important prognostic factors in breast cancer. At the time of diagnosis, patients are usually > 50 years old or in a postmenopausal period. According to SEER (Surveillance, Epidemiology and End Results) data, the mean age for breast cancer is 61 years; breast cancer incidence between the ages of 45–54, 65–74, 75–84 and for 85 and older are 22.6, 19, 15.8 and 5.6%, respectively [9]. In a Turkish study, the mean age of breast cancer was 51.5 and the incidence rates for the age groups of 41–50, 51–70 and > 70 years

Table 1. Clinical features of the patients studied

Clinical features of the patients	
Total number of the patients, n	522
Patients older than 69 years, n (%)	35 (6.7)
Mean age, years	74.5
Mean tumor size, cm	1.9
Stage at diagnosis, n (%)	
Stage I	24 (68.6)
Stage IIA	11 (31.4)
Grade, n (%)	
1	15 (42.8)
2	16 (45.7)
3	4 (11.4)
Adjuvant therapy modalities, n (%)	
Group 1 (BCS+HT)	21 (60)
Group 1a (T1N0M0)	16 (76.2)
Group 1b (T2N0M0)	5 (23.8)
Group 2 (BCS+HT+RT)	4 (11.4)
Group 3 (BCS+CT+HT+RT)	10 (28.6)
Mean follow-up period, months	
Group 1	32.2
Group 2	31.3
Group 3	20.4
Breast cancer-specific mortality, n	0
Local recurrence, n	0

BCS = Breast conserving surgery, HT = hormonal therapy, RT = radiotherapy, CT = chemotherapy.

were 31, 40.7 and 8.2%, respectively [10]. In our study, the incidence for early stage breast cancer for the patients older than 69 years was 6.7%.

Compared with younger patients, the elderly rarely have higher grade tumors. ER and progesterone receptor (PR) positivity are more common in elderly patients than in the premenopausal group. The ER positivity rate was 60% when considering all ages, but 70–95% in patients > 70 years [11]. In Pierga's study, 81% of 1,755 operable breast cancer patients older than 75 years showed a lower proliferation index but a higher rate of hormone-related tumors [12]. In our study, all patients were HR positive and 31 (88.6%) had tumors of grade 1 or 2.

BCS is the standard procedure suggested for every patient who has a small, early stage tumor. Many randomized control studies prove that it is as effective as mastectomy in elderly patients with early stage breast cancer [13]. For this group of patients, no differences in survival time or disease-free life expectancy were found for these treatment methods [14]. In addition, BCS offers a better life quality. In our study, BCS + SLNB was given to all of our patients. At least 70–80% of breast cancers in patients older than 65 years are HR positive. For this reason, all ER- and PR-positive elderly patients should be assessed for adjuvant endocrinological therapy after surgery [15–17].

HT has an evident effect on survival rates in all patients, and 5-year therapy with TMX in HR-positive women older than 50 has a more positive effective on survival and relapse rate than CT. In addition, TMX decreases breast cancer occurrence rates by 40–50%. 5-year-adjuvant TMX therapy decreases the annual cancer-related mortality rate by 31%. In 66–88-year-old women, HT extends the 15-year-survival period by 21% [18, 19].

While TMX used to be the only accepted adjuvant HT agent, nowadays AIs such as anastrozole, letrozole and exemestane present new horizons in treatment [20]. The choice of adjuvant agent has to be made considering recurrence risk, tumor biology and potential side effects. Studies comparing efficiency of TMX and AIs in early stage breast cancer show that AIs provide a longer disease-free life period but only a slight difference in survival rate [21]. Anastrozole lengthens disease-free life period, delays recurrence, decreases end-

organ metastasis and contralateral cancer genesis in postmenopausal patients [22]. AIs are also more effective in patients older than 75 years [23]. AIs have also been shown to be more effective than TMX in the postmenopausal population.

Standard surgical treatment is suggested for appropriate elderly patients and AI can be used as adjuvant HT to provide regional control in these patients. In the study of Martelli et al., patients of ≥ 70 years clinically shown to have a single N0 tumor of ≤ 3 cm received BCS; no adjuvant RT was given to patients who had negative surgical borders, and no axillary procedures were applied. A median 15-year follow-up of their patients who were given adjuvant TMX showed a local recurrence of only 8% in the same breast [6]. In another study including patients of ≥ 60 years with tumors of ≤ 1 cm that were HR positive, regional recurrence rates after BCS when RT was or was not applied were 1.2% and 0%, respectively, after a median follow up period of 5.6 years [7]. In the study of Hughes et al., BCS was applied to patients of ≥ 70 years with tumors of ≤ 2 cm. Patients, displaying either surgically negative or HR-positive tumors, were then randomized to 1 of 2 treatment arms: 1 applying adjuvant RT to the breast and the other not. All patients received TMX for 5 years. At the median 5-year follow-up, the regional recurrence rate for patients receiving RT was 1%, and for those not receiving RT, 4%. The 5-year overall survival rates were similar (87 and 86%, respectively) [24]. These data show that, in patients of 70 years or older with tumors of ≤ 2 cm, if the surgical borders of excised specimen are intact and hormonal expressions are positive, there is no need to apply adjuvant RT after BCS [25, 26].

In our study, no cancer-specific mortality or local recurrence was seen during the 27.9-month follow-up in any of the groups. The BCS+HT regimen seems to be an efficient treatment option for early stage breast cancer in appropriate 70-year or older patients (small grade 1 tumors, relatively older age groups).

Disclosure Statement

The authors have no conflicts of interest to declare

References

- 1 Louwman WJ, Vulto JCM, Verhoeven RHA, et al.: Clinical epidemiology of breast cancer in the elderly. *Eur J Cancer* 2007;43:2242–2252.
- 2 Muss HB: Adjuvant treatment of elderly breast cancer patients. *Breast* 2007;16 Suppl 2, S159–S165.
- 3 Tang SW, Parker H, Winterbottom L, et al.: Early primary breast cancer in the elderly – Pattern of presentation and treatment. *Surg Oncol* 2011;20:7–12.
- 4 Wyld L, Reed M: The role of surgery in the management of older women with breast cancer. *Eur J Cancer* 2007;43:2253–2263.
- 5 MacDonald BK, Cockerell OC, Sanders WAS, et al.: The incidence and lifetime prevalence of neurological disorders in a prospective community based study in the UK. *Brain* 2000;123:665–676.
- 6 Martelli G, Miceli G, Costa A, et al.: Elderly breast cancer patients treated by conservative surgery alone plus adjuvant tamoxifen: 15-year results of a prospective study. *Cancer* 2008;112:481–488.
- 7 Fyles AW, McCready DR, Manchul LA, et al.: Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. *N Engl J Med* 2004;351:963–970.
- 8 Güllüoğlu BM: Surgical treatment of breast cancer in elderly; is current evidence strong enough to implement less aggressive treatment modalities? *Ulusal Cerrahi Dergisi* 2009;25:78–81.
- 9 Howlader N, Noone AM, Krapcho M, et al. (eds): SEER Cancer Statistics Review, 1975–2008, National Cancer Institute, Bethesda, MD http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011.
- 10 Ozmen V: Breast cancer in the world and Turkey. *J Breast Health* 2008;2:7–12.

- 11 Diab SG, Elledge RM, Clarke GM: Tumour characteristics and clinical outcome of elderly women with breast cancer. *J Natl Cancer Inst* 2000;92:550–556.
- 12 Pierga JY, Girre V, Laurence V, et al.: Characteristics and outcome of 1755 operable breast cancers in women over 70 years of age. *Breast* 2004;13:3969–3975.
- 13 Wyld L, Reed M: The role of surgery in the management of older women with breast cancer. *Eur J Cancer*. 2007;43:2253–2263.
- 14 DeHaes JCJM, Curran D, Aaronson NK, et al.: Quality of life in breast cancer patients aged over 70 years, participating in the EORTC 10850 randomised clinical trial. *Eur J Cancer* 2003;39:945–951.
- 15 Balducci L: Treating elderly patients with hormone sensitive breast cancer. What do the data show? *Cancer Treatment Rev* 2009, 35:47–56.
- 16 Reed M. W, Audisioy A, Wyld L: The role of surgery in the treatment of elderly women with breast cancer. *Clin Oncol* 2009;21:103–110.
- 17 Giorgano SH, Hortobagyi GN, Kau SWC, et al.: Breast cancer treatment guidelines in older women. *J Clin Oncol* 2005;23:783–791.
- 18 Hind D, Wyld L, Beverley CB, et al.: Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus). *Cochrane Database Syst Rev* 2006;1:CD004272.
- 19 Fennessy M, Bates T, MacRae K, et al.: Late follow-up of a randomized trial of surgery plus tamoxifen versus tamoxifen alone in women aged over 70 years with operable breast cancer. *Br J Surg* 2004;91:699–704.
- 20 Monica M, Gautam J, David AP: Anastrozole use in early stage breast cancer of post-menopausal women. *Clin Med Ther* 2009;1:141–156.
- 21 Howell A, Cuzick J, Baum M, et al.: Effect of anastrozole and tamoxifen as adjuvant treatment for early stage breast cancer: 100-month analysis of the ATAC trial. *Lancet Oncol* 2008;9:45–53.
- 22 BIG 1–98 collaborative group: Letrozole therapy alone or in sequence with tamoxifen in women with breast cancer. *N Engl J Med* 2009;8:766–776.
- 23 Seruga B, Tannock IF: Up-front use of aromatase inhibitors as adjuvant therapy for breast cancer: The emperor has no clothes. *J Clin Oncol* 2009;6:840–842.
- 24 Hughes KS, Schnaper LA, Berry D, et al.: Lumpectomy plus tamoxifen with or without irradiation in women over 70 years of age or older with early breast cancer. *N Engl J Med* 2004;351:971–977.
- 25 Fisher B, Anderson S, Bryant J, et al.: Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–1241.
- 26 Blichert-Toft M, Nielsen M, Duing M, et al.: Long-term results of breast conserving surgery vs mastectomy for early stage invasive breast cancer: 20-year follow-up of the Danish randomized DBCG-82TM protocol. *Acta Oncol* 2008;47:672–681.