Omission of adjuvant radiation therapy in elderly patients with low risk breast cancer undergoing breast-conserving surgery - two center experience

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Introduction. Breast cancer is, now often diagnosed in patients older than 70 years due to longer life expectancy. The usual treatment is mastectomy to obviate radiotherapy or breast-conserving surgery followed by radiotherapy. The aim of this study was to investigate the need for adjuvant radiotherapy in older patients and the consequences of omitting radiotherapy following conservative surgery.

Methods. An extensive database search was made of patients who had been treated for breast cancer at the Department of Oncology, University Hospital Olomouc and the Atlas Hospital in Zlin (2004-2008). We identified 738 patients of whom 190 patients (25.7%) were older than 70 years of age. These were followed up for progression-free and overall survival. The cause of death was checked for breast cancer relapse.

Results. In total only 9 patients undergoing breast saving surgery were ultimately identified. No patient had confirmed local recurrence during the follow up period: Two patients have died due to distant metastasis without local relapse and one patient has died for reasons other than breast cancer.

Conclusion. Omitting radiotherapy after breast saving surgery provides an opportunity for women to undergo breast saving surgery and avoid 7 weeks of radiotherapy. This could significantly improve patient quality of life. In our of many years experience and from published randomized data, this procedure is safe for a select group of patients 70 years of age and older.

Key words: breast cancer, radiation-therapy, elderly patients

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INTRODUCTION

Breast cancer is the most common malignancy (excluding skin cancer) in women in the Czech Republic with an incidence in 2009 of 62.5 new cases per 100,000. This is slowly increasing due to an aging population and the screening which was launched in the Czech Republic in 2004 and led to rapid increase in the diagnosis of early stage breast cancer[1]. About one third of all breast cancers are diagnosed in populations over 70 years of age[2,3]. The generally accepted procedure in these patients is to either mastectomy to avoid radiotherapy or breast saving surgery followed by radiotherapy. Both are followed by chemotherapy, targeted therapy or hormonal therapy according to stage of disease and revailing risk factors. Breast cancer in older populations presents more often with favorable biologic characteristics such as Luminal A disease (Estrogen or/and progesterone receptor positive defined as hormonal positivity over 5%, proliferative index Ki 67 under 14%, lower histological grade – Grade 1 or 2, Her -2 negative disease). Adding the adjuvant radiotherapy after breast saving surgery significantly decreases the recurrence rate in the population of patients with breast cancer[5] however, due to the low aggressiveness of breast cancer presenting in older patients, the presence of concurrent diseases, performance status, lower life expectancy, radiotherapy morbidity and the duration of the radiotherapy often requiring hospitalization due to travel issues in older patients often causes significant psychosocial and functional impairment. We considered omitting radiotherapy in these patients if the tumor has low risk characteristics and the patient will be treated with hormonal therapy alone after the surgery. This procedure is also accepted as by the National Comprehensive Cancer Network[6] based on published data[7-8] and is considered as evidence Category 1 (Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate).

METHODS

We performed an extensive database search of patients treated at the Department of Oncology, University Hospital Olomouc and at the Department of Surgery, Atlas Hospital Zlin from 2004 until 2008 and identified 738 patients undergoing breast conserving surgery of whom 190 patients (25.7%) were considered elderly (older then 70 years of age). After review of this population only 9 eligible patients were identified (4.7%). We collected the pathological data, and followed up eligible patients regarding adjuvant treatment, recurrence rate and overall survival. In cases where the patient had died, we contacted the general practitioner to check the exact cause of death to rule out possible cancer progression if no specific cause of death was identified from databases of oncology departments.

According to the documentation available, the possibility of avoiding radiotherapy was discussed with patients and patients agreed to proceed without radiotherapy. In the case of clinical suspicion, additional examinations were performed. In the case of death, the specific cause of death was investigated by contacting the treating physician. We also included patients in higher disease stages but the patients rejected adjuvant radiotherapy for personal reasons. In such case patients were asked to sign the informed consent. Median follow up was calculated using Microsoft excel program.

Table 1. Age of the patients and stage of the disease at diagnosis.

Patient nr.	Age at diagnosis (years)	Stage of the disease
1	88	I A
2	74	IA
3	72	IA
4	74	IA
5	77	IA
6	71	IA
7	84	II A
8	72	IIIC
9	71	IA

RESULTS

Adjuvant radiotherapy together with surgery procedure plays a major role in local control of the disease. The primary endpoint of our study was the number of local breast cancer recurrences as failure of local treatment. The extensive database search in breast cancer patients treated at the Department of Oncology, University Hospital Olomouc and Department of Surgery, Atlas Hospital Zlin over the years 2006 and 2010 indentified 9 patients undergoing breast-conserving surgery without adjuvant radiotherapy (in 8 patients quadrantectomy was performed, 1 patient underwent lumpectomy, in 8 patients sentinel node biopsy was performed and in one case the axillary dissection was followed due to positive sentinele node, in one case no SNB or axillary dissection was performed). The anamnestic, pathologic and surgical characteristics of patients included and procedures performed are summarized in Tables 1, 2 and 3. Patients were checked-up every 3 months in the first 3 years, every 6 months for each additional 2 years and yearly thereafter. These follow ups were performed by a clinical oncologist. During the follow up, yearly mammography was performed to rule out local relapse, yearly chest X-rays, and yearly abdominal ultrasounds to rule out distant metastasis were performed. All patients were examined by medical oncologists to detect signs of local or distant metastasis. Also tumor markers – Ca 15-3 and Carcinoembryonic antigen were assessed at every visit. Other examinations were ordered according to clinical findings. From 9 patients after a median follow up of 50 months, 3 patients died (cause of death in the first patient was congestive hearth failure without disease relapse confirmed by the treating general practitioner and in the second and third patients, death was caused by distant metastases of the breast cancer without clinical or radiologic evidence of local relapse). No local relapse was identified during the follow up. Two patients did not fulfill our inclusion criteria. However since they rejected the adjuvant radiation and signed informed consent about possible risks, they were also be included and assessed (1 patient with pN3 nodal disease, 1 patient with negative hormonal receptors and size of the tumor over 2 cm) even if all patients undergoing breast-conserving surgery were counseled about the need for adjuvant ra-

Table 2. Pathological characteristics of the tumors.

Patient nr.	Histology	Size (mm)	Grade	ER/PR status	Her- 2 status	Ki67
1	ductal invasive	20	2	poz/poz	neg 0	15%+
2	ductal invasive	12	2	poz/poz	neg 0	2%+
3	ductal invasive	8	2	poz/neg	neg 1+	10%+
4	papillary invasive	6	2	poz/poz	neg 0	5%+
5	ductal invasive	18	2	poz/poz	poz 3+	15-20%+
6	papillary invasive	15	2	poz/poz	neg 0	5-10%+
7	ductal invasive	25	3	neg/neg	neg 0	100%+
8	ductal invasive	25	3	poz/neg	neg 0	40%+
9	lobular invasive	20	2	poz/neg	neg 1+	25%+

Table 3. Surgical procedures performed.

Patient nr.	Breast procedure	Axillary procedure
1	quadrantectomy	SNB
2	quadrantectomy	SNB
3	quadrantectomy	SNB
4	quadrantectomy	SNB
5	lumpectomy	SNB
6	quadrantectomy	SNB
7	quadrantectomy	no axillary procedure
8	quadrantectomy	SNB/axillary dissection
9	quadrantectomy	SNB

SNB – sentinel node biopsy, SNB/axillary dissection – positive SNB for tumor tissue was followed by axillary dissection

diotherapy after surgery and mastectomy was offered in the case patient would not accept radiotherapy. All patients with hormone positive disease received adjuvant hormonal therapy (tamoxifen or aromatase inhibitor) for 5 years and one patient with pN3 adjuvant chemotherapy followed by hormonal therapy as well.

DISCUSSION

The aim of this paper was to highlight the possibility of safely omitting radiation therapy in early stage low risk breast cancer in older (+70) patients undergoing breast-conserving surgery. Both institutions treat over 400 patients per year and approximately 20-30% of these patients are over 70 years of age, it is clear from the database search that the option of not irradiating the elderly is underused. There are data clearly demonstrating that not radiating patients after breast conserving surgery increases the risk of local relapse. There are no data describing the quality of life of patients after mastectomy and comparing them to data after breast- conserving procedures However from our longstanding experience there is a clear and constantly increasing preference of even older women for breast saving procedures.

Fisher et al. investigated if lumpectomy with or without radiation therapy increases the relapse rate compared to mastectomy for the treatment of invasive breast cancer. In this study there were 1851 patients and the conclusion was that relapse rate in unirradiated women was 39.2% compared with 14.3% in the women who underwent lumpectomy and breast irradiation (P<0.001). There was no significant difference in overall survival[9]. Cooke et al. performed a retrospective study with 97 node positive breast cancer patients recruited from the London Regional Cancer Center. These patients were randomized to breast-conserving surgery followed by Tamoxifen with or without radiation therapy. After 39 months of follow up, the recurrence rate was 5% in radiated versus 21% in unirradiated women (P=0.0388). However, no difference in cause death was found, concluding that radiation therapy in women after 70 years of age may not be necessary[10]. Veronesi et al. recruited 579 women in a trial comparing quadrantectomy with axillary dissection with or without radiation therapy. Again the local relapse rate was significantly higher in the arm without radiotherapy 23.5% compared with 5.8%, however this difference was more significant in women under 45 years of age and decreased in patients older 65. Regarding the overall survival the same as in previous studies overall survival curves did not differ significantly (P=0.326) (ref.[11]).

Similar results particularly in overall survival were published in many other studies[12-15] concluding the benefit of adjuvant radiotherapy for patients over 70 years of age seems to be very low and avoiding radiotherapy may be a safe procedure. In contrast to the above mentioned papers, there are studies which have proven that omitting radiation therapy may significantly increase local recurrence rate and breast cancer deaths. EBCTCG meta-analysis of individual patient data for 10 801 women from 17 randomized trials of radiotherapy versus no radiotherapy after breast-conserving surgery concluded that the recurrence rate without adding radiotherapy increased from 15.6% to 31.0% and also the radiotherapy reduced the breast cancer death rate by about a sixth[16]. Considering all these studies there is no clear evidence for the benefit of radiation therapy for older (+70) population and medical judgment should be used when considering risk and benefits of adding adjuvant radiation therapy after breast-conserving surgery or indicating mastectomy. Further research will be needed to clearly compare the psychosocial consequences of mastectomy compared with slightly increased risk of local relapse rate without the clear evidence for decreased overall survival.

Another rapidly growing possible method to solve the above-described situation is accelerated breast irradiation. This involves using fewer, larger-dose radiation or brachytherapy techniques to achieve the same effect. There are currently many trials which are assessing the effectiveness and safety of this procedure[17-22]. However, from preliminary data it seems reasonable to consider these methods as a valid alternative to omitting adjuvant radiotherapy in elderly patients with early stage breast cancer.

The limitation of our study is the low number of patients which indirectly points to the fact that breast-conserving surgery not followed by radiotherapy, is usually omitted by treating physicians without specific reason and patients either undergo mastectomy or in the case of breast saving surgery, radiotherapy is indicated.

CONCLUSION

There are no clear recommendations regarding RT in elderly patients and omission of RT should be considered based on an individual assessment of the overall condition of the patient, associated diseases, complications caused by daily transportation to the RT unit and the personal preferences of the patient.

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