European Journal of Surgical Oncology 44 (2018) 951–956

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Omitting radiotherapy in women ≥ 65 years with low-risk early breast cancer after breast-conserving surgery and adjuvant endocrine therapy is safe☆

Åsa Wickberg [a, *], Göran Liljegren [a], Fredrika Killander [b], Henrik Lindman [c], Judith Bjöhle [d], Michael Carlberg [e], Carl Blomqvist [f], Johan Ahlgren [e], Kenneth Villman [e]

[a] Department of Surgery, Faculty of Medicine and Health, SE-701 82, Örebro, Sweden
[b] Skåne University Hospital and Lund University, Lund, Sweden
[c] Akademic Hospital, Uppsala University, Uppsala, Sweden
[d] Karolinska Institutet and University Hospital, Stockholm, Sweden
[e] Department of Oncology, Faculty of Medicine and Health, SE-701 82, Örebro, Sweden
[f] Department of Oncology, Helsinki University, Finland

ARTICLE INFO

Article history:
Accepted 5 April 2018
Available online 13 April 2018

Keywords:
Breast-conserving surgery
Endocrine therapy
Postoperative radiotherapy

ABSTRACT

Purpose: The aim of this study was to verify if radiotherapy (RT) safely can be omitted in older women treated for estrogen-receptor positive early breast cancer with breast-conserving surgery (BCS) and endocrine therapy (ET).

Patients and Methods: Eligibility criteria were: consecutive patients with age ≥65 years, BCS + sentinel node biopsy, clear margins, unifocal T1N0M0 breast cancer tumor, Elston-Ellis histological grade 1 or 2 and estrogen receptor-positive tumor. After informed consent, adjuvant ET for 5 years was prescribed. Primary endpoint was ipsilateral breast tumor recurrence (IBTR). Secondary endpoints were contralateral breast cancer and overall survival.

Results: Between 2006 and 2012, 603 women were included from 14 Swedish centers. Median age was 71.1 years (range 65–90). After a median follow-up of 68 months 16 IBTR (cumulative incidence at five-year follow-up; 1.2%, 95% CI, 0.6% to 2.5%), 6 regional recurrences (one combined with IBTR), 2 distant recurrences (both without IBTR or regional recurrence) and 13 contralateral breast cancers were observed. There were 48 deaths. One death (2.1%) was due to breast cancer and 13 (27.1%) were due to other cancers (2 endometrial cancers). Five-year overall survival was 93.0% (95% CI, 90.5% to 94.9%).

Conclusion: BCS and ET without RT seem to be a safe treatment option in women ≥ 65 years with early breast cancer and favorable histopathology. The risk of IBTR is comparable to the risk of contralateral breast cancer. Moreover, concurrent morbidity dominates over breast cancer as leading cause of death in this cohort with low-risk breast tumors.

© 2018 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

Introduction

Breast-conserving surgery (BCS) is the standard treatment for early breast cancer. The addition of postoperative radiotherapy (RT) has, in a large meta-analysis, been shown to halve the rate of local recurrences and reduce the breast cancer death by about a sixth [1]. However, the absolute benefits from RT vary substantially according to patient- and tumor-characteristics. There are subgroups of women where the adverse effects of RT, for instance ischemic heart disease and lung cancer [2–4], may exceed the advantages of postoperative RT, especially for long-term smokers [5]. Moreover, some women may choose a mastectomy in order to avoid 3–5 weeks of RT. After adjustment for age, among women with breast cancer in USA, the likelihood of receiving RT following BCS decreased significantly with increasing travel distance to the

☆ The study has previously been presented as a poster at the breast cancer conference in San Antonio, December 2016.

* Corresponding author. Department of Surgery, University Hospital Örebro, S-701 85 Örebro, Sweden.
E-mail address: asa.wickberg@regionorebrolan.se (Å. Wickberg).

https://doi.org/10.1016/j.ejso.2018.04.002
0748-7983/© 2018 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

nearest radiation-treatment facility [6]. Assessment of the consequences of omitting RT for patients diagnosed with early-stage breast cancer is therefore needed.

We defined a cohort of women with low-risk-tumors were we presumed that the risk of IBTR after breast-conserving surgery with the addition of endocrine therapy (ET), even in the absence of postoperative RT would be at most 1–2% per year or 10% at 10 years.

Methods

Study design and patient baseline characteristics

The study was designed as a multicenter national prospective cohort study. Between 2006 and 2012, 603 women from 14 Swedish centers were included in the study. Every woman was carefully informed about pros and cons of the treatment and after written informed consent, adjuvant ET for 5 years was prescribed. All women included were registered in a case report form (CRF), which was sent to a local manager at the Clinical Research Support, University Hospital Örebro. Two patients did not fulfill the inclusion criteria (due to age <65 years) and were excluded from the cohort.

Eligibility criteria were; consecutive patients with age ≥65 years, BCS (sector resection and sentinel node biopsy) with clear margins (no tumor cells at inked border for invasive cancer, 2 mm margin for in situ cancer), T1N0M0 non-lobular breast cancer tumor, Elston-Ellis histological grade [7] 1 or 2 and estrogen receptor (ER) positive and/or progesterone receptor (PR) positive tumor. For every woman, information was collected from the CRF regarding initial treatment and tumor characteristics; type of adjuvant endocrine therapy (tamoxifen (TAM) or aromatase inhibitors (AI)), tumor size, histopathological type, Elston-Ellis histological grade, ER, PR and human epidermal growth factor receptor 2 (HER2). All variables were prospectively registered in the CRF (Table 1).

Follow-up

The procedures included mammography performed annually or more often when indicated by clinical symptoms. Annual visit with a physician was not mandatory, but the women were instructed to contact the treating institution in case of suspicion of recurrence.

Table 1
Baseline characteristics. Calculated from the 601 participants.

	Median (range)
Age, years	71 (65–90)
Tumor size, mm	11.0 [3–20]
	N (%)
Endocrine therapy	
tamoxifen	534 (88.9)
aromatase inhibitor	67 (11.1)
Histopathology	
ductal	534 (88.9)
Other[a]	67 (11.1)
NHG	
grade I	342 (56.9)
grade II	258 (42.1)
unknown	1 (0.17)
Progesterone rec	
positive	536 (89.1)
negative	63 (10.5)
unknown	2 (0.33)
Her-2	
positive	11 (1.8)
negative	531 (88.4)
unknown	59 (9.8)

[a] Mucinous, papillary, tubular.

All IBTR's were confirmed by histopathology. Every year confirmed recurrences, cancers of other origin, discontinuation or change of ET or withdrawal from the study had to be reported to the CRS from each participating center.

A safety committee consisting of one statistician and two physicians, who were not involved in the study, examined all reported events once a year. If the IBTR exceeded 2% per year the study protocol recommended closure of the study.

The study was approved by the Regional Ethical Review Board at Uppsala University, D n r 2005:321. It was also registered in the data base “Research and Investigations in Sweden” (N r 53991).

Endpoints and outcome assessment

Primary endpoint was ipsilateral breast tumor recurrence (IBTR). Secondary endpoints were contralateral breast cancer and overall survival. Most of the women had a complete follow-up until 2017-03-01 (or could be followed until death), but 31 women were lost to follow-up. All women who were lost to follow-up were included in the analysis until withdrawal.

Statistics

It was decided that a ten year rate of IBTR of 10% would be acceptable. The number of included cases enabled estimation of IBTR with approximately 5% accuracy. E g, if 600 patients were enrolled with an estimated IBTR of 8% at ten years then the corresponding 95% CI would be 5.7% to 10.3%. The cumulative incidence of IBTR was estimated by a competing risk regression model implemented in Stata 12.1 (Stata/SE for Windows; Stata Corp, College Station TX), with regional recurrence, distant metastases, other types of cancers and deaths as competing risk [8]. The same procedure was done with respect to contralateral breast cancer. Overall survival was estimated with the Kaplan-Meier method. 95% confidence intervals (CI) were used for all calculations.

Results

Median age was 71.1 years (range 65–90) and the median tumor size was 11 mm. Only 1.8% of the women had tumors with overexpression of HER2 and 10.5% of the tumors were progesterone receptor negative. All tumors were ER-positive. The majority of the tumors were of ductal origin, low grade and PR-positive. Most of the patients received TAM (Table 1).

IBTR and other new primary tumors

At a median follow-up of 68 months (range 2 days–120 months) 16 IBTR, 6 regional recurrences (one combined with IBTR) and 2 distant recurrences both without IBTR or regional recurrence were observed. The calculated cumulative incidence of IBTR at five years was 1.2% (95% CI, 0.6% to 2.5%) (Fig. 1). Inclusion of the two excluded women did not change the estimate.

Thirteen women had a contralateral breast cancer; cumulative incidence at five years 1.8% (95% CI 0.9–3.2) (Fig. 3).

Thirty-four patients were diagnosed with tumors of other origins. Three of these tumors were ovarian cancer, three were lung cancer, nine were gastrointestinal cancer, eleven were other types of cancer and eight were endometrial cancers. Seven of the women with endometrial cancer were treated with TAM and one woman had an AI. However, one woman had TAM for only two weeks. For the others the duration range of intake was 1.5–7 years.

Download English Version:

https://daneshyari.com/en/article/8786668

Download Persian Version:

https://daneshyari.com/article/8786668

Daneshyari.com