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Original research

Short-course radiotherapy in elderly women with breast cancer: Comparison by age, comorbidity index and toxicity

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ABSTRACT

Background: Breast cancer is the most common malignancy amongst elderly women. It represents the main cause of mortality for those women and it is steadily increasing. The primary therapeutic approach remains surgery, as in other age groups. The role of radiotherapy following surgery is still debated. The use of hypofractionated schedules is challenging the standard fractionation and has now been considered an advantageous option within this subgroup of patients. Results from randomized controlled trials have not been shown to be inferior to standard fractionation in terms of local recurrence, disease-free survival and overall survival. Acute and late side effects were not increased by hypofractionated regimens.
Patients and methods: 60 elderly women treated by hypofractionated radiotherapy after breast conserving surgery were stratified by age. Comorbidities associated compliance and toxicity correlation to age were the first endpoints of the study. Comorbidity associated compliance was calculated by Cumulative Illness Rating Scale Geriatric.
Results: At a median follow-up of 15 months overall survival was 100%, without severe late toxicity. No statistical significant differences were found between Cumulative Illness Rating Scale-Geriatric, systemic therapy and toxicity.
Conclusion: In our experience hypofractioned regimens seem to be safe and reliable in the elderly setting, although longer follow up is needed.

1. Introduction

Breast cancer is the most common malignancy amongst elderly women and the main cause of mortality. The incidence of breast cancer in elderly women and its management is going to be one of a major public health problem in the next few years [1,2].

Even in the absence of a general consensus, it is commonly considered that people >65 are old. The degree is extremely variable and several different subgroups can be observed in relation to performance status, to presence of comorbidities, to conditions of social distress [3].

Age is the most important risk factor in breast cancer occurrence. The relative risk for breast cancer increases by 5.8 times in

List of abbreviations: RT, radiotherapy; HyRT, hypofractionated radiation therapy; Gy, gray; ASTRO, American Society of Therapeutic Radiation Oncology; GEC-ESTRO, European Society of Radiotherapy and Oncology; NCI, National Cancer Institute; NCCN, National Comprehensive Cancer Network; CIRS-G, Cumulative Illness Rating Scale Geriatric; CT, Computed Tomography; RTOG, Radiation Therapy Oncology Group; CTCAE, common terminology criteria of adverse events; SIOG, International Society of Geriatric Oncology; EUSOMA, European Society of Breast Cancer Specialists.

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women aged 65 and more compared with younger women [4]. Approximately 45% of breast cancer occurs in over 65 years old women and 33% are occur in those aged >70 years [1].

Despite these data older women are often excluded from screening [5,6]; in addition the patients from older age groups are included in few randomized studies to assess the effectiveness of therapies. This means that the appropriate treatment for the elderly is still being debated [7]. 40% of older women have at least a factor of comorbidity (cardiovascular diseases, preexisting cancer, diabetes mellitus and dementia) at the time of diagnosis, even if the analysis of the relationship between age, comorbidity and cancer treatment shows that almost all of the patients are able to tolerate appropriate therapy at the presentation of tumor [8]. For these reasons (absence of screening program at this age, later diagnosis, inadequate treatment and comorbidity), there has not been observed in the elderly setting the same reduction in mortality reported in young women [9–13]: relative survival at 5 and 10 years of patients >70 years is lower than that of patients aged between 40 and 70 years, even when adapted to the stage of presentation of the disease; socio-economic conditions and the unequal access to health care may contribute to the worse prognosis [14]. The first therapeutic approach in breast cancer remains surgery, as in other age groups. Meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) [15] shows that radiation treatment after conservative surgery reduces the risk of local recurrence and results in a benefit in survival, regardless of age. However, the absolute benefit on survival in elderly is limited because of the presence of more comorbidity factors. According to National Comprehensive Cancer Network (NCCN) guidelines, the administration of boost is considered optional in relation to the presentation of the disease, because the absolute benefit in this patient population may be limited [16–18]. Some studies have evaluated, in patients older than 70 years treated with conservative surgery, low risk, receptor-positive, the possibility of omitting the radiotherapy(RT). Higher local recurrence rates were observed in these studies when omitting RT (9% versus 2% [19], 7.7% versus 0.6% [20], 5.7% versus 0.5% [21], 4% vs 1% [18]).

The use of hypofractionated radiotherapy (HyRT) is challenging the standard fractionation and has now been considered an advantageous option within this subgroup of patients. According to the National Cancer Institute (NCI) hypofractionated radiotherapy can be defined as radiation treatment in which the total dose of radiation is divided into large doses and treatments are given once a day or less often. Hypofractionated radiation therapy is given over a shorter period of time (fewer days or weeks) than standard radiation therapy. HyRT schedules (42.56Gy/16 fractions), as an alternative to conventional schedules, have been tested in large multicentre randomized trials and have shown to be either equivalent or not inferior to standard RT (60Gy/30fractions) in terms of local tumor control, patient survival and late post-radiation effects [24,29]Acute and late side effects were not increased by hypofractionated regimens. [17,22–28], that have been proven to be safe and effective.

The first endpoint of the study was comorbidities associated compliance and toxicity correlation to age was the first endpoint of the study. elderly women given adjuvant HyRT after breast conserving surgery.

2. Patients and methods

60 elderly patients diagnosed with primary early breast cancer were given adjuvant HyRT between 20011 and 2013. All patients were consented for HyRT according to the Helsinki Declaration. Institutional Review Committee approved the study. The treatment schedule was 42,56 Gy in 16 fractions (2.66 Gy/day) on whole breast volume without boost. Inclusion criteria for participation met ASTRO evidence based guidelines [25]. Patients demographics and tumor characteristics are listed in Table 1.

Patients underwent breast conserving surgery and adjuvant treatments were discussed and scheduled by post-operative multidisciplinary meetings. 56 out of 60 patients (93.3%) were given adjuvant endocrine therapy; 5 out of 60 patients (8.3%) were scheduled for anthracycline and taxane based chemotherapy, none of the patients to biological therapy. Comorbidities were recorded by the Cumulative Illness Rating Scale Geriatric Version (CIRS-G) [30–32]. This scoring system measures the presence of chronic disease ("morbidity"), taking into account the severity and differentiates between fourteen organ systems, as shown in Table 1.

Every comorbidity of a patient was assigned to one of the organ systems and rated from 1 (mild comorbidity) to 4 (extremely severe comorbidity).

The general rules for severity are:

0 → No problem affects that system.
1 → mild problem or past significant problem.
2 → moderate disability or morbidity and/or require first-line therapy.
3 → serious problem and/or disability and/or difficult to control chronic problems constant and significant.
4 → extremely serious and/or immediate treatment required and/or organ failure and/or severe functional impairment.

The final overall score can vary theoretically from 0 to 56 (although a very high score is not possible).

A Computed Tomography (CT) scan was performed in for each patient from sixth cervical vertebrae to 5 centimetres (cm) below the diaphragm. CT axial scanning was performed at 0.25 cm intervals. For this purpose a *Toshiba Aquilion* scanner was used. The positioning was mentioned by using breast support system. Patients were placed in the supine position with arms above the head, hands holding the contralateral elbows and head opposed to the target breast. Whole breast reference volume and organs at risk (lung, heart, contralateral breast) were contoured by using Radiation Therapy Oncology Group (RTOG) guidelines. PTV was created from the whole breast reference by excluding 0.5 cm of skin surface. The plans were optimized with Eclipse system (Varian, Palo Alto, CA) by using 6 MV photon beams. The calculation model was AAA algorithm with a 5 mm calculation grid. Gantry and collimator angles were adjusted to minimize organs at risk from irradiation, whilst maximizing target volume coverage. Two equally weighted tangential fields were used. Field-in-field technique was required in order to obtain a homogeneous dose distribution to the whole breast for those patients presenting with anatomy and/or breast size issues. The prescribed dose was 42,56 Gy in 16 fractions (2.66 Gy/day). The whole breast received less than 107% of the prescribed dose and no more than 5% of the whole breast volume received less than 95% of the prescribed dose. Dose constraints for heart and ipsilateral lung and contralateral breast were V5Gy<10%, V17Gy < 7% andV10Gy < 5%, respectively.

Radiation treatment started within 8–12 weeks after breast conservative surgery or 21–30 days after systemic adjuvant chemotherapy. Acute dermal toxicity was assessed according to RTOG Acute Radiation Morbidity Scoring Criteria. Late toxicity was assessed by using Common Terminology Criteria of Adverse Events (CTCAE) v3.0 of the NCI which is composed of 13 items: 3 related to subjective symptoms (flushing, itching, and pain) and 10 relating to the examination objective [34]. SOMA/LENT toxicity scale was used to score arm lymphedema [35,36]. Comorbidity index was assessed. Overall survival and disease –free survival were estimated. .