RESEARCH ARTICLE

HYPOFRACTIONATED RADIOTHERAPY OF BREAST CANCER IN ELDERLY WOMEN

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Abstract

Introduction: Breast cancer remains the first malignant pathology in women and its diagnosis in elderly women is late. The aim of our work is to evaluate the effectiveness of hypofractionated radiotherapy in the treatment of breast cancer in elderly women.

Material And Methods: This is a retrospective study of 171 patients aged over 65 years followed for invasive breast cancer and who received adjuvant hypofractionated radiotherapy at the radiotherapy department of CHU Hassan II Fez from January 2012 to December 2016.

Results: The frequency of breast cancer in women aged over 65 years was 7.31%. The average age of our patients was 70 years (65-88 years) of which 40% were older than 70 years. 8.5% of patients had a family history of breast cancer. The delay of consultation was 10 months. A breast nodule was the revealing sign in all patients with inflammatory signs in 4.6%; axillary adenopathy was found in 20% of patients. All cancers were histologically proven. The cancer was infiltrating ductal in 90% of cases. 27% of the tumors were Scarff-Bloom and Richardson grade I, 45% grade II, 30% grade III. Hormone receptors were expressed in 77% and HER positive in 10% of patients. 83% underwent mastectomy with lymph node dissection followed by adjuvant radiotherapy according to the hypo-fractionated protocol: total dose of 42 Gy on the wall, of which 32% of patients also received lymph node irradiation, fractionation 2.8 Gy/ Fr in 15 sessions, spread over 19 days 17% of the patients had conservative surgery associated with adjuvant external radiotherapy on the breast according to the same scheme with a boost of 11.8 Gy on the tumor bed, spread over 25 days. After a median follow-up of 5 years, overall survival was estimated at 84.2%, locoregional recurrence-free survival at 84.7% and metastatic recurrence-free survival at 83%. Acute toxicity consisted of radiodermatitis in 81% of patients, and post-radiation fibrosis in 15%, and no long-term cardiac or pulmonary toxicity was observed.

Conclusion: For elderly patients, adjuvant hypofractionated irradiation seems to be a good alternative, with a good rate of local control, and without increased toxicity.

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Introduction:
Adjuvant radiotherapy remains essential in the treatment of early-stage cancers, reducing the risk of locoregional cancer recurrence and breast cancer deaths, including in patients with positive lymphnodestreated with mastectomy and axillary dissection.

For several decades, adjuvant radiation therapy programs for these patients have delivered 25 fractions of 2 Gy over 5 weeks. Randomized controlled trials with long-term follow-up have since confirmed that fewer and larger fractions, giving a lower total dose, are at least as safe and effective as the previously used international standard (1).

Material and Methods:
This is a retrospective study, involving 171 patients aged over 65 years followed for invasive breast cancer and who received hypofractionated adjuvant radiotherapy at the radiotherapy department of CHU Hassan II Fez from January 2012 to December 2016.

Patients received three-dimensional adjuvant radiotherapy according to the hypofractionated protocol: total dose of 42 Gy on the wall of which 32% of patients also received lymphnode irradiation, fractionation 2.8 Gy/ Fr in 15 sessions.

Statistical analyses were performed with SPSS version 20 software. The analyses of OS, SSRL PFS and DFS were estimated by the Kaplan-Meier method, and the cox method was used for multifactorial analysis.

Results:
Our patients were women older than 65 years with invasive breast carcinoma (pT1-4, pN0-3, M0) after complete microscopic excision of the primary tumor by breast-conserving surgery or mastectomy. All patients underwent axillary surgery (sentinel node biopsy or axillary dissection).

| Table I: Patient characteristics. |
|----------------------------------|
| Features                         | Number of patients (n=171 )(%) |
| Age (years)                      |                               |
| Median                           | 70 (65-88)                    |
| Under 70 years                   | 103 (60)                      |
| Over 70 years                    | 68 (40)                       |
| Laterality n (%)                 |                               |
| Left / Right                     | 60 (35)/ 111 (60)              |
| Histological type n (%)          |                               |
| Invasive ductal                  | 154 (90)                      |
| Lobular infiltrating             | 10 (7)                        |
| Other                            | 7(3)                          |
| Histological grade               |                               |
| SBR I                            | 46 (27)                       |
| SBR II                           | 77 (45)                       |
| SBR III                          | 51(30)                        |
| Presence of vascularemboli       | 46 (27)                       |
| Hormone receptors                |                               |
| Positive                         | 132 (77)                      |
| Her2Neu (%)                      |                               |
| Positive                         | 18 (11)                       |
| Negative                         | 153 (89)                      |
| T pathology (AJCC 2010)          |                               |
| T1                               | 32(19)                        |
| T2                               | 101(59)                       |
| T3                               | 26(15,4)                      |
The patients received three-dimensional adjuvant radiotherapy according to the hypo-fractionated protocol: total dose of 42Gy on the wall of which 32% of the patients also received lymph node irradiation, fractionation 2.8Gy/Fr in 15 sessions (Figure 1).

**Figure 1:** Axial scan section showing the dose distribution during chest wall irradiation.
Survival and relapse:
After a median follow-up of 5 years, overall survival is estimated at 84.2% (Figure 2); locoregional recurrence-free survival at 84.7% and metastatic recurrence-free survival at 83%.

![Figure 2: Overall survival curve.](image)

IC: (67.5-76.12), m = 71.86

Toxicity:
Acute toxicity consisted of radiodermatitis in 81% of patients, and post-radiation fibrosis in 15% patients, and no long-term cardiac or pulmonary toxicity was observed.

| skin toxicity | Number (%) | Type and grade |
|---------------|------------|----------------|
| acute         | 139 (81)   | radiodermatitis:|
|               |            | Grade 1: 85(61%) |
|               |            | Grade 2: 51(37%) |
|               |            | Grade 3: 3(2%) |
| chronic       | 36 (21%)   | Fibrosis: 14% |
|               |            | Telangiectasia: 7% |
|               |            | Hyperpigmentation: 1% |

Table II: Distribution of patients by toxicity.

Discussion:
Our objective was to determine whether whole-breast irradiation after conservative surgery or mastectomy could be safe and effective when delivered at a higher dose per fraction and over a shorter period of time in elderly women than in the standard regimen.

Standard treatment delivering 50 Gy in 25 fractions to the breast or wall and or not to the lymphnodes and or not to the tumorbewith 10 to 16 Gy of additional radiation in conventional fractionation is relatively long and restrictive, especially for elderly patients and/or patients with long tracts (2). In 2000, in a study in the United States, Athas et al. showed that up to 33% of women treated with conservative surgery did not receive the adjuvant radiotherapy they should have had, mainly because of age over 70 years and distance to the radiotherapy center [3].
Various accelerated and non-accelerated hypofractionated irradiation regimens have been tested to address this issue. Data from four large phase III non-inferiority trials, showed, with level of evidence IA, that hypofractionated breast radiotherapy was non-inferior to normofractionated radiotherapy, both in terms of efficacy and toxicity [4-6].

The randomized phase III Fast-Forward trial showed non-inferiority of the 27Gy and 26Gy 5-fraction regimens compared with 40Gy 15-fraction regimen, with the incidence of local relapse at 5 years after hypofractionated radiotherapy given in five fractions being no lower than the standard 3-week regimen. The 26 Gy dose level is similar to the 40 Gy 15-fraction dose level in terms of patient-rated normal tissue effects, clinician-rated normal tissue effects, and breast appearance change. The consistency of the FAST-Forward results with previous hypofractionation trials supports the adoption of 26 Gy in five daily fractions as the new standard for women with operable breast cancer requiring adjuvant radiation therapy (1).

Since 2011, the American Society of Radiation Therapy (ASTRO) has published recommendations for the use of hypofractionated regimens, in patients at least 50 years of age, with stage pT1-2, pN0 breast cancer, without adjuvant chemotherapy, with no indication for additional tumor bed irradiation [7]. Since then, several national and international guidelines have also followed [8-14]. In the United Kingdom, as in many other countries, 40 Gy in 15 fractions has become the standard treatment for breast or even parietal irradiation, with or without lymph node irradiation [15].

Conclusion:-
In this series evaluating a hypofractionated regimen in elderly patients with invasive breast carcinoma, the results are promising both in terms of locoregional control and toxicity. This hypofractionated regimen allows to decongest the treatment machines and to shorten the waiting time for our patients.

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