Cancer/Radiothérapie 20 (2016) 292–298

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Original article

Breast-conserving treatment for ductal carcinoma in situ: Impact of boost and tamoxifen on local recurrences

Traitement radiochirurgical conservateur des cancers canalaires in situ : influence du boost *et du tamoxifène sur les récidives locales*

B. Cutuli[a,*], N. Wiezzane[b], I. Palumbo[c], P. Barbieri[d], M. Guenzi[e], A. Huscher[f], S. Borghesi[g], C. Delva[h], T. Iannone[i], E. Vianello[a,j], M.-E. Rosetto[k], C. Aristei[c]

[a] *Institut du cancer Courlancy, 38, rue de Courlancy, 51100 Reims, France*
[b] *Centre Georges-François-Leclerc, 1, rue du Pr-Marion, 21000 Dijon, France*
[c] *Radiation Oncology Section, University and General Hospital of Perugia, Perugia, Italy*
[d] *Policlinico di Modena, Modena, Italy*
[e] *Azienda Ospedaliera Universitaria, Genova, Italy*
[f] *Fondazione Poliambulanza, Brescia, Italy*
[g] *Ospedale San Donato, Arezzo, Italy*
[h] *Sylia-Stat, Bourg-la-Reine, France*
[i] *Ospedale San Martino, Belluno, Italy*
[j] *Ospedale SS San Giovanni e Paolo, Venezia, Italy*
[k] *Ospedale Belcolle, Viterbo, Italy*

ARTICLE INFO

Article history:
Received 23 August 2015
Received in revised form 2 April 2016
Accepted 5 April 2016

Keywords:
DCIS
Treatment
Breast-conserving therapy
Boost
Tamoxifen
Local recurrence
Nuclear grade

ABSTRACT

Purpose. – Ductal carcinoma in situ represents 15 to 20% of all breast cancers. Breast-conserving surgery and whole breast irradiation was performed in about 60% of the cases. This study reports local recurrence rates in patients with ductal carcinoma in situ treated by breast-conserving surgery and whole breast irradiation with or without boost and/or tamoxifen and compares different therapeutic options in two European countries.

Patients and methods. – From 1998 to 2007, 819 patients with pure ductal carcinoma in situ were collected, both in France (266) and Italy (553). Median age was 56. All underwent breast-conserving surgery and whole breast irradiation; 391 (48%) received a boost (55% in France and 45% in Italy, $P = 0.017$) and 173 (22.5%) tamoxifen (4.5% in France and 32% in Italy, $P < 0.0001$).

Results. – With a 90-month median follow-up, there were 51 local recurrences (6.2%), including 27 invasive (53%). The 5- and 10-year local recurrence rates were 4% and 8.6%. Two patients developed axillary recurrence and 12 (1.5%) metastases (seven after invasive local recurrence); 41 (5%) patients had contralateral breast cancer. In the multivariate analysis, high nuclear grade and lack of tamoxifen are the most powerful predictors of local recurrence, with 2.6 (95% confidence interval [95% CI]: 1.74–3.89, $P = 0.0012$) and 2.85 (95% CI: 1.42–5.72, $P = 0.04$) odds ratio (OR) estimates, respectively. Age, margin status and boost did not influence local recurrence rates.

Conclusions. – This study confirms the ductal carcinoma in situ treatment heterogeneity among countries and the unfavourable prognostic role of nuclear grade. Tamoxifen reduces local recurrence rates and might be considered for some subgroups of patients, but further confirmation is required. The boost usefulness still remains unclear.

* Corresponding author.
E-mail address: bcutuli@iccreims.fr (B. Cutuli).

http://dx.doi.org/10.1016/j.canrad.2016.04.004
1278-3218/

RÉSUMÉ

Mots clés :
Carcinome canalaire in situ
CCIS
Traitement
Chirurgie conservatrice
Boost
Tamoxifène
Récidive locale
Grade nucléaire

Objectif de l'étude. – Évaluation du taux de récidive locale parmi les patientes traitées pour un carcinome canalaire in situ par chirurgie conservatrice et irradiation mammaire avec ou sans *boost* et/ou tamoxifène, et comparaison des modalités thérapeutiques entre deux pays européens.
Patientes et méthodes. – Les dossiers de 819 patientes recevant un traitement pour un carcinome canalaire in situ pur, en France et en Italie entre 1998 et 2007, ont été analysés. L'âge médian était de 56 ans. Toutes ont été traitées par chirurgie conservatrice et irradiation ; 391 (48 %) ont reçu un *boost* (55 % en France et 45 % en Italie, $p = 0{,}017$) et 173 (22,5 %) du tamoxifène (4,5 % en France et 32 % en Italie, $p < 0{,}0001$).
Résultats. – Avec 90 mois de suivi médian, 51 récidives locales sont survenues (6,2 %). Les taux de récidive locale à 5 et 10 ans étaient respectivement de 4 % et 8,6 %. Deux rechutes axillaires, 12 disséminations métastatiques (1,5 %, sept après une récidive locale invasive) et 41 cancers du sein controlatéraux (5 %) ont été observés. En analyse multifactorielle, le haut grade nucléaire et l'absence de tamoxifène étaient les plus importants facteurs prédictifs de récidive locale avec des risques relatifs respectifs de 2,6 (intervalle de confiance à 95 % : 1,74–3,89, $p = 0{,}0012$) et 2,85 (1,42–5,72, $p = 0{,}04$). L'âge, l'état des marges et la réalisation d'un *boost* n'ont pas influencé le taux de récidive locale.
Conclusions. – Cette étude confirme l'hétérogénéité des traitements des patientes atteintes d'un carcinome canalaire in situ dans les différents pays et le pronostic défavorable lié au grade nucléaire. Le tamoxifène réduit le taux de récidive locale et pourrait être proposé dans certains sous-groupes de patientes, mais cela nécessite des confirmations supplémentaires. L'utilité du *boost* reste encore incertaine.

1. Introduction

In Western countries, ductal carcinoma in situ represents 15 to 20% of all breast cancers [1]. Due to disease extension and/or multicentricity, 30–35% of the patients, especially young women, need mastectomy [2,3]. For smaller lesions, four large randomized trials and a meta-analysis showed that breast-conserving surgery followed by whole breast irradiation allows optimal local control [4–8]. Consequently, several national guidelines (e.g. National Comprehensive Cancer Network, French) recommend lumpectomy and whole breast irradiation as primary treatment (without lymph node surgery). However, treatment modalities remain heterogeneous among countries [9–11], with wide variations in boost and tamoxifen use [12–16], due to various perceptions of ductal carcinoma in situ by many physicians, ranging from very "indolent" to "potentially invasive", often without a clear scientific support. Invasive local recurrence is a crucial problem in ductal carcinoma in situ and leads to 10–15% long-term metastatic evolution [4,5,11]. Both randomized trials and retrospective studies identified local recurrence risk factors after breast-conserving surgery and whole breast irradiation, but several series present various biases with heterogeneous results [2,4–7,12–14].

In order to compare the daily clinical practice in two European countries and to analyse local recurrence risk factors, we assessed the results after breast-conserving surgery and whole breast irradiation in a cohort of 819 patients with ductal carcinoma in situ coming from France and Italy.

2. Patients and methods

2.1. Study design and data collection

From 1998 to 2007, 819 patients were collected in two centres (one comprehensive cancer centre and one private clinic) in France ($n = 266$, 33%) and seven (four academic and three local hospitals) in Italy ($n = 553$, 67%).

A detailed form including demographic and clinical data, histopathological features (size, nuclear grade, margin status, hormone receptor and Her-2 status), and treatments (breast and axilla surgery, radiotherapy and hormonal therapy) was used. All events were calculated from first surgery data; local recurrence corresponds to an in situ or invasive carcinoma in the treated breast. Nodal recurrences were defined as biopsy-proven carcinoma or clinical evidence of disease in the ipsilateral axilla, supraclavicular or internal mammary nodes. Distant metastasis corresponds to radiological and/or pathological evidence of disease at any distant site. Contralateral disease was biopsy-proven (in situ or invasive) carcinoma in the other breast.

2.2. Statistics

Analyses were performed with SAS software (version 9.2, SAS Institute Inc., Cary, NC). To compare two groups, we used the Chi^2 test for categorical variables, *t*-test for continuous variables and non-parametric Mann-Whitney test when the assumption of normality was questionable. To compare more than two groups, we used the Chi^2 test for categorical variables, a one-way analysis of variance for continuous variables and non-parametric Kruskal–Wallis test when the assumption of normality was questionable. Multiple logistic regression analysis was performed to identify local recurrence risk factors. A stepwise procedure was used to select variables. Stepping is stopped when there are no further candidate variables entering in the model at a 5% significance level. The odds ratio and its 95% confidence interval (95% CI) were also calculated.

3. Results

3.1. Demographic characteristics

Median age was 56.4 years (range: 32–84 years), with 24.3% of the patients under 50, 67.2% from 50 to 70 and 8.5% over 70; 556 out of 736 evaluable patients (75%) were postmenopausal.

3.2. Discovery modalities

Ductal carcinoma in situ was discovered by mammography, clinical symptoms or both in 88%, 3% and 9% of the cases, respectively.