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Original article

## Outcome of postmastectomy radiotherapy after primary systemic treatment in patients with clinical T1-2N1 breast cancer<sup>☆</sup>

*Bénéfice de la radiothérapie après une mastectomie et une chimiothérapie néoadjuvante chez les patientes atteintes de cancer du sein de stade T1-2N1*

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### ARTICLE INFO

#### Article history:

Received 7 February 2017

Received in revised form 23 July 2017

Accepted 31 July 2017

#### Keywords:

Breast cancer

Primary systemic treatment

Postmastectomy radiotherapy

Recurrence

### ABSTRACT

**Purpose.** – The role of postmastectomy radiotherapy following primary systemic treatment in patients with clinical T1-2N1 breast cancer remains a controversial issue. The purpose of this study was to evaluate the benefit of postmastectomy radiotherapy following primary systemic treatment.

**Patients and methods.** – Between 2005 and 2012, in two independent institutions, female patients with T1-2N1 breast cancer receiving primary systemic treatment followed by mastectomy and lymph node dissection because bad response, then treated with or without chest wall and regional lymph node irradiation have been studied retrospectively. The patients received normofractionated radiotherapy using 3D conformal photons or electron techniques. Locoregional recurrence-free survival, distant metastasis-free survival and disease-free survival were calculated using Kaplan-Meier method. Univariate analysis of potential prognostic factors was performed using log-rank test.

**Results.** – Eighty-eight patients have been studied. Of them, 75 patients received postmastectomy radiotherapy. At surgery, 53 patients achieved ypN0. Median follow-up was 67 months. Postmastectomy radiotherapy significantly improved locoregional recurrence-free survival, with a 5-year rate of 96.9% versus 78.6% in the group that did not have postmastectomy radiotherapy. In the subgroup of 53 patients achieving ypN0, postmastectomy radiotherapy improved locoregional recurrence-free survival (a 5-year rate of 94.7% vs. 72.9%), distant metastasis-free survival (a 5-year rate of 92.8% vs. 75%) and disease-free survival (a 5-year rate of 92.9% vs. 62.5%). By univariate analysis, postmastectomy radiotherapy was the only significant prognostic factor affecting locoregional recurrence-free survival.

**Conclusions.** – For patients with clinical T1-2N1 disease, postmastectomy radiotherapy could significantly improve locoregional recurrence-free survival after primary systemic treatment and be even more therapeutic in the subgroup of patients with good response for primary systemic treatment by improving locoregional recurrence-free, distant metastasis-free and disease-free survival. Larger prospective studies are needed to confirm our findings.

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<sup>☆</sup> A part of this work was accepted for presentation in the poster viewing session in ASTRO's 58th Annual Meeting in Boston.

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<https://doi.org/10.1016/j.canrad.2017.07.051>

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R É S U M É

**Mots clés :**  
Cancer du sein  
Chimiothérapie néoadjuvante  
Radiothérapie  
Mastectomie  
Récidives

**Objectif de l'étude.** – L'intérêt de la radiothérapie après une chimiothérapie néoadjuvante et une mastectomie chez des patientes atteintes de tumeur de stade T1-2N1 reste parfois discuté. L'objectif de cette étude était d'évaluer le bénéfice de ce traitement dans cette population de patientes.

**Patientes et méthodes.** – Entre 2005 et 2012, dans deux hôpitaux, des patientes atteintes d'un cancer du sein de stade T1-2N1 ont été prises en charge par une chimiothérapie néoadjuvante, suivie d'une mastectomie et curage en raison d'une réponse insuffisante. Ensuite, certaines patientes ont reçu une irradiation postopératoire dans la paroi thoracique et d'autres non, selon les protocoles de l'hôpital et leurs désirs. Les patientes qui ont reçu une irradiation, l'ont été dans la paroi thoracique et les ganglions avec des techniques conformationnelles tridimensionnelles de photons et/ou d'électrons. Les taux de survie sans récurrence locorégionale, la survie sans métastase et la survie sans maladie ont été calculés selon la méthode de Kaplan-Meier. Le Log rank test a été utilisé pour évaluer les facteurs pronostiques.

**Résultats.** – Soixante-quinze des 98 patientes ont reçu une irradiation après la mastectomie et le curage. Après la chimiothérapie, 53 cancers étaient de stade ypN0. Le suivi médian était de 67 mois. La radiothérapie postopératoire a amélioré significativement les probabilités de survie sans récurrence avec à 5 ans un taux de 94,7 % dans le groupe irradié, contre 72,9 % chez les patientes non irradiées. Les taux de survie sans métastases étaient de 92,8 % chez les patientes irradiées et 75 % chez les patientes non irradiées, ceux de survie sans maladie à 5 ans à respectivement de 92,9 % contre 62,5 %. L'analyse unifactorielle a trouvé comme seul facteur pronostique la radiothérapie postopératoire.

**Conclusion.** – Pour les patientes atteintes de tumeur de stade T1-2N1, après une chimiothérapie néoadjuvante et une mastectomie, la radiothérapie améliore les résultats en termes de contrôle locorégional et de survie. De plus grandes études prospectives sont nécessaires pour confirmer les résultats.

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## 1. Introduction

The primary systemic treatment is increasingly used in the early stage breast cancer [1,2]. The advantages of primary systemic treatment include that it can reduce the extent of surgery and increased breast conservation therapy eligibility [3]. In case of bad local response, multiple lesions, and impossible breast conserving surgery, the mastectomy is still a treatment of choice [4]. It was shown, that in case on lymph nodes positive disease, there is a benefit of the regional lymph nodes irradiation following mastectomy in terms of local control as well in terms of survival benefit [5–7].

However, even in the adjuvant setting, the value of postmastectomy radiotherapy in patients with T1-2 and one to three positive lymph nodes has remained an issue of controversy until now [8,9]. In general, the population of patients treated with mastectomy is of high risk because the bad response to primary systemic treatment and the impossibility to realize the breast conserving surgery. There is no enough data concerning the place of postmastectomy radiotherapy correlated to the pathological response to primary systemic treatment. No prospective data is available for ypN0 patients. The decisions of adjuvant radiotherapy following primary systemic treatment are largely derived from prospective studies in the adjuvant setting [5,6,10–13]. The aim of this retrospective study was to evaluate the benefit of postmastectomy radiotherapy following primary systemic treatment and mastectomy in patients with cT1-2N1 disease.

## 2. Patients and methods

### 2.1. Patients

We studied retrospectively population of consecutively treated female patients with cT1-2N1 breast cancer who received primary systemic treatment followed by mastectomy between January 2005 and December 2012 in our two hospitals. Patients with distant metastases, more than four positive lymph nodes after primary systemic treatment, inflammatory or bilateral breast cancer,

previous or concurrent malignancy (except for non-melanoma skin cancers) were excluded. In total, 88 patients met the inclusion criteria and were involved in this study. The initial clinical stage was determined by physical examination combined with imaging studies. All patients underwent mammography and ultrasound of breast as well as an ultrasound evaluation of regional lymph nodes. This study was approved by the institut Curie Breast Cancer Study Group and Ruijin Hospital, Shanghai Jiaotong University School of Medicine Review Board, and waiver of consent was obtained.

### 2.2. Treatment modalities

#### 2.2.1. Surgery

All patients underwent mastectomy. No immediate breast reconstruction has been allowed. Axillary lymph node dissection was realized in most cases.

#### 2.2.2. Systemic treatment

All patients received preoperative taxanes and/or anthracyclines based chemotherapy. Some of the patients received adjuvant systemic treatment after the surgery. All patients with hormonal receptor positive tumours received endocrine treatment. Trastuzumab was given in most patients with HER2 positive tumours.

#### 2.2.3. Radiotherapy

Most of the patients received postmastectomy radiotherapy of chest wall and regional nodes. Dose prescription was 50 Gy in 25 fractions. The chest wall was treated with three-dimension conformal radiotherapy technique field-in-field using photons [14]. The regional nodes were treated with an anterior mixed photon and electron beam. The volume delineation and definition were realized according to the Radiation Therapy Oncology Group (RTOG) guidelines [15].

#### 2.2.4. Statistical analysis

Pathologic complete response was defined as no residual invasive cancer in the breast and regional nodes following primary

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