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Accelerated partial breast irradiation for elderly women with early breast cancer: A compromise between whole breast irradiation and omission of radiotherapy

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ABSTRACT

PURPOSE: Regarding adjuvant radiation therapy making decision for elderly women, Albert (2013) published a nomogram predicting the mastectomy-free survival (MFS) rate with or without adjuvant irradiation. Based on this approach, we proposed to investigate the use of accelerated partial breast irradiation (APBI) vs. whole breast irradiation (WBI) or endocrine therapy alone in elderly low-risk breast cancer patients.

METHODS AND MATERIALS: For each elderly woman treated by conserving surgery and APBI (multicatheter interstitial high-dose-rate brachytherapy), 5- and 10-year MFS rates were calculated. For each treated patient, using the Albert nomogram, we calculated the estimated MFS rates at 5 and 10 years, with and without WBI. Then, we compared the estimated MFS rates after no irradiation and WBI vs. observed MFS rates after APBI.

RESULTS: From 2005 to 2016, 79 patients were treated. Median followup was 96.8 months [68.6−104.9], median age was 77 years [66−89]. Expected 5- and 10-year mastectomy rates calculated with the Albert nomogram without WBI were 2.95% and 7.25%, respectively, leading to a 10-year MFS rate of 92.7%. Expected 5- and 10-year mastectomy rates after WBI were 1.41% and 3.66%, respectively, leading to a 10-year MFS rate of 96.3%. Regarding observed MFS rate, 1 pt (1.3%) experienced a salvage mastectomy. The 10-year MFS rate after APBI was 97.4% vs. 96.3% after WBI ($p = 1$) and 92.7% after no irradiation ($p = 0.27$). No toxicity Grade 3 or more was observed.

CONCLUSIONS: APBI seems to be an attractive compromise between WBI and no irradiation for elderly women with early stage breast cancer as far as local control, quality of life and cost benefit is concerned.

Keywords: Breast cancer; Elderly; Radiation therapy; Accelerated partial breast irradiation

Introduction

Breast cancer has been recognized as a major public health problem for many years (1). Currently, life expectancy is growing, and the incidence of breast cancer increases with advancing age. This situation could explain in part that more than 40% of breast cancers occur in women over 65 years (2). In the United States, an increase of 57% in breast cancer is estimated over the next 2 decades (3).

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Conflict of interest: The authors declare that they have no competing interests.

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A meta-analysis of randomized studies with 10,801 patients showed that radiotherapy (RT) after breast-conserving surgery reduces the risk of all recurrences including ipsilateral breast tumor recurrence and improves overall survival by increasing breast cancer−specific survival (4). But, specifically for elderly women, whole breast irradiation (WBI) which can last 6−7 weeks or 4−5 weeks in case of hypofractionated regiment may be difficult to perform due to their potential comorbidities and the treatment inconveniences (numerous transportations…) (5−7). To reduce discomfort and expenses induced by adjuvant irradiation, in low-risk breast cancer (elderly/postmenopausal women), three randomized trials comparing adjuvant endocrine therapy alone with or without postoperative external WBI were conducted. They confirmed that combined treatment does not significantly impact on overall survival rate, whereas it significantly reduces the rate of local recurrence (8−12). Based on these results, the National Comprehensive Cancer Network concluded that RT could be omitted in women aged 70 and older with estrogen receptor (ER) positive, Stage I breast cancer receiving endocrine therapy (even if the noncompliance with endocrine therapy is often observed) (13).

Is it possible to propose a compromise between WBI (long but efficient treatment in terms of local control) and endocrine therapy as sole adjuvant treatment (more comfortable for the elderly but significantly risky in terms of local recurrence)? Could accelerated partial breast irradiation (APBI) considered as an attractive answer to this question, decreasing the risk of local recurrence rate while in the same time, preserving quality of life for the patient and expenses for healthcare reimbursement system (14)?

To help elderly patients and clinicians in adjuvant radiation therapy decision making, dedicated nomograms were proposed. Based on different prognostic criteria such age, race, tumor size, hormonal receptor status, and axillary lymph node status, Albert *et al.* (15) built a nomogram predicting the mastectomy-free survival (MFS) rate with or without adjuvant irradiation. Based on this approach, we proposed to investigate the use of APBI vs. WBI or endocrine therapy alone in elderly low-risk breast cancer.

Methods and materials

Nomogram

Albert *et al.* (15) developed a nomogram to predict the likelihood of long-term breast preservation with and without WBI. With a median followup of 7.2 years, the cohort included 16,092 elderly patients (pts) (66−79 years old) with invasive breast carcinoma. More than 90% of treated women were white with a majority of pT1 tumors. The nomogram included every predictive factor of time to mastectomy on multivariate analysis, which are age, race, tumor size, ER status, and receipt of RT with or without nodal disease. For our study, we used those variables from our population of only white women treated by breast conserving surgery and APBI to estimate the 5- and 10-year MFS rates. For each treated patient, using the Albert nomogram, we calculated the estimated MFS rates at 5 and 10 years, with and without WBI. Then, we compared the estimated MFS rates after no irradiation and WBI vs. observed MFS rates after APBI. This protocol was approved by the central review board of the Antoine Lacassagne Cancer Center.

Patient's features

From 2005 to 2016, in the Antoine Lacassagne Cancer Center, we included patients who underwent conservative surgery for early breast cancer followed by APBI (multicatheter high-dose-rate interstitial brachytherapy) according to the Groupe Européen de Curiethérapie de l'European Society for Radiotherapy and Oncology (GEC-ESTRO) and American Society for Radiation Oncology (ASTRO) recommendations (16, 17). Eligibility criteria were T1−T2 (up to 3 cm), N0, M0, and clear excision margins (≥2 mm for invasive ductal carcinoma and ≥5 mm for invasive lobular carcinoma). Grade 3 histologic features or lymphovascular invasion were accepted, but not both. Exclusion criteria were patients younger than 66 years, history of previous *in situ* or invasive breast cancer of ipsilateral breast. Because the population used for the Albert nomogram focused on women between 66 and 79 years old with invasive carcinoma, we removed patients with *in situ* carcinoma and younger than 66 years. However, we accepted women older than 79 years. Written consent after complete information of each patient was necessary.

Breast surgery was performed under general anesthesia. Nodal status was known using sentinel lymph node biopsy with extemporaneous examination. In case of node invasion, an axillary dissection was performed. An extemporaneous examination was also done after lumpectomy to confirm malignancy-free excision margins. The tumor bed was closed after using four to five surgical clips on each side of the lumpectomy cavity with one of them deeply clamped to pectoral muscle.

Brachytherapy procedure used catheters (Sharp Needles; Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) which were inserted intraoperatively into the tumor bed for all the patients, according to the Paris system geometric rules (spacing of 12−15 mm between two adjacent catheters in the same plan and 10−12 mm between plans) (18). Once the final pathological results confirmed the indication of APBI, CT-scan planification was performed. The clinical target volume (CTV) was delineated with a safety margin of 2 cm from the clips minus the surgical margins described by the pathologist in every direction. The CTV was redefined as 5 mm below the skin surface and 5 mm above the underlying ribs. The planification was performed using Plato then OncentraBrachy treatment planning systems (Nucletron, Elekta AB, Stockholm, Sweden). Dose−volume adaptation was manually achieved