

Organ-saving Surgery After Preoperative Radiotherapy in Patients with Breast Cancer

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Abstract

Breast-conserving surgery (BCS) followed by an adjuvant radiation therapy (RT) and chemotherapy is considered the preferred approach in patients with I-II stage breast cancer [1]. If radiation is effective anticancer treatment modalities why it used after removing of breast cancer?

Objective: To analyze the results of BCS in breast cancer patients (pts) who underwent the neoadjuvant chemo-radiation treatment.

Methods. In the retrospective study were involved 36 women with primary breast cancer of stage T1 (19 pts) and T2 (18 pts). Molecular subtypes: luminal A – 16 pts, luminal B – 5, HER2-neu – 8, triple negative – 7 pts. Treatment scheme: neo-adjuvant radiation- or chemo-radiation therapy, BCS with axillary lymph node dissection, postoperative radiation- / chemo- / hormonal therapy was depending of histological finding, age, hormonal status, and risk factors. RT (Terabalt-100, Co-60): neoadjuvant whole-breast irradiation 30–35 Gy/ 2.6-2.9 Gy per daily fraction or 5 Gy per fraction × 5 days. Results. There were no serious postop wound complications. The grade 1-2 arm lymphedema occur in 3 (8%) pts. Slight breast edema and grade 1 radio-dermatitis was observed in half of the pts. Cosmetic appearance of the breast was good and satisfactory a few months after surgery. Reoperation due to a local recurrence was done in two cases (5.5%). 4 (11%) pts died 2-4 years after surgery due to metastatic disease. 5-years overall survival rate was 89 %.

Conclusions. BCS can be safely performed after neo-adjuvant chemo- and radiation therapy. Preoperative RT of breast cancer is safe and does not impact significantly on postoperative wound complications.

Keywords: breast cancer, neoadjuvant radiotherapy, breast-conserving surgery

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Introduction

It is now well known that radiation therapy (RT) after mastectomy or breast-conserving surgery reduced local recurrence, and even demonstrated that it improved survival [1].

Radiation therapy achieves its therapeutic effect by inducing different types of cancer cell death. The major cell death mechanisms involved in radiation therapy are programmed cell death (apoptosis), mitotic cell death (mitotic catastrophe), necrosis, senescence (permanent loss of cell proliferative capacity) and autophagy. The main goal of radiation therapy is to deprive cancer cells of their multiplication potential and eventually kill the cancer cells. Cancer cells whose DNA is damaged beyond repair stop dividing and die. Radiation therapy does not kill cancer cells right away. It takes hours, days or weeks of treatment before cancer cells start to die. From the theoretical point of view it is conceivable that neoadjuvant radiotherapy applied to breast cancer activates a local antitumor immunity [2–8].

Breast-conserving surgery (with or without neoadjuvant chemotherapy) followed by an adjuvant radiation therapy and chemotherapy is considered the preferred approach in patients with I-II stage breast cancer. Postoperative radiations consist of the several approaches – whole breast irradiation (with or without boost), partial breast radiotherapy and radiotherapy of regional lymphatics [9–11]. On this basis, the question arises: What is the point of application for postoperative radiation therapy if the cancer absent, was removed?

Objective: To analyze the results of breast preservation surgery and demonstrate the safety of radiation therapy in breast cancer patients who underwent the neoadjuvant chemo-radiation treatment.

Materials and methods

In the retrospective study were involved

36 women with breast cancer who were treated in the Ternopil Oncology Center, Ukraine in 2010–2017 years. Age distribution: 5 (14 %) patients were 25–40 years old, 21 (58 %) pts – 41–60 y.o., 10 (28 %) pts – were over 60 y.o. The primary sizes of tumors were from 15 mm to 50 mm. Breast cancer at stage T1 was diagnosed in 19 (53 %) pts, stage T2 – in 18 (47 %) pts; N1 lymphnode metastases were in 4 (11 %) pts. Molecular subtypes: luminal A – 16 (44 %) pts, luminal B – 5 (14 %) pts, HER2-neu – 8 (22 %) pts, triple negative – 7 (20 %) pts.

Treatments:

- neo-adjuvant radiation- or chemo-radiation therapy,
- breast-conserving surgery (BCS) with axillary lymph node dissection of the level I/II,
- adjuvant (postoperative) radiation- / chemo- / hormonal therapy was depending of histological finding, age, hormonal status, and risk factors.

Methods of radiotherapy (Terabalt-100: Co-60 gamma-irradiation): neoadjuvant whole-breast irradiation 30–35 Gy. Part of patients (26 pts) had breast irradiation with 2.6–2.9 Gy per daily fraction for 11–14 days; another group (10 pts) had short preoperative irradiation with 5 Gy per fraction × 5 days, and surgery on the next 1–2 days. Postoperative RT to the tumor bed 25–30 Gy with 2.2 Gy daily fractions as usually begins 2–3 months after BCS, and total dose of breast RT consist of 50–60 Gy. In cases of favorable prognosis or complete pathological response (pCR) of tumor, the adjuvant RT was omitted.

Chemotherapy: AC, CAF 2–4 cycles in neoadjuvant and adjuvant regimes. In patients with HER2-neu positive tumor the trastuzumab and paclitaxel were used. Endocrine therapies were used in cases of hormone receptor positive tumors.

Results

The results of BCS after neo-adjuvant chemo-radiation therapy are illustrated on the

two clinical cases below (fig. 1–6).

Clinical case 1

Patient M., 38 years old, was diagnosed with right breast cancer cT2NxM0. Initial tumor was 50×33 mm by ultrasound and mammographic measurement, axillary lymphnodes – 16 mm. Treatment: neoadjuvant chemo- (Doxorubicin – Cyclophosphamide, ×3 cycles) and radiation therapy (whole breast irradiation – 36.5/2.8 Gy, and axilla – 31.5/2.6 Gy). As results of neoadjuvant treatment breast cancer shrinks to 15×12 mm, that gave possibility to carried out BCS (fig. 1-2); the axillary lymphnode dissection was done by separate incision. Breast surgery carried out on 20th day after last fraction of RT, and on

10th day after 3rd cycle of chemotherapy. Histological exam: invasive ductal (scirrhous) carcinoma, G3; free margins of resection; hyperplasia of lymph nodes. IHC: ER++, PR+, Her2neu+++, luminal-B subtype breast cancer (triple positive). Postoperative diagnosis: cancer of the right breast pT2pN0M0pG3, luminal B.

Adjuvant treatment consists of 2 cycles of chemotherapy (AC) and partial breast irradiation on tumor bed (24.2 Gy/ 2.2 Gy per fraction). This postoperative radiation was possible only 2 months after BCS. The endocrine treatment: tamoxifen 5 years, and hysterectomy with ovariectomy due to uterine fibroids (in two years after BCS). No local recurrence or distant metastases within six years follow-up of patient.



Fig.1. *Clinical case 1*. Patient M., 38 y/o: after the neo-adjuvant chemoradiation therapy. The dose of radiation: 36.5 Gy on breast, and 31.5 Gy on axilla. Scheme of surgical incisions for breast conserving operation with axillary dissection



Fig.2. Surgical specimen "on table"



Fig.3. Operated breast two years later. No signs of previous radiotherapy (60.7 Gy) for the breast

Clinical case 2

Patient L., 48 years old, with cancer of left breast cT2NxM0 was administrated the systemic neoadjuvant treatment: 4 cycles of chemotherapy (AC), and RT for the left breast 38.9 Gy/2.6 Gy, and axilla 30 Gy/2.4 Gy.

As results of neoadjuvant treatment breast cancer shrinks from 28 mm to 15 mm, the size of axillary lymph nodes were 12 mm. Breast-saving surgery – partial breast resection with regional lymph node dissection

(fig. 4-5) was done on 40th day after finishing of RT, and on 21st day after 4th cycle of chemotherapy. Histology: invasive ductal (scirrhous) carcinoma, G2; “free” resection margins; hyperplasia of lymphatic nodes. IHC: ER++, 78%, PR++, 69%, Her2neu–: luminal-A breast cancer. Postop diagnosis: cancer of the left breast pT2pN0M0pG2, luminal A.

Endocrine therapy (tamoxifen, AI) was a further treatment for several years. No any recurrence of disease after 5 years follow-up.



Fig.4. *Clinical case 2*. Patient L., 48 y/o: scheme of planning surgery after the neo-adjuvant chemoradiation therapy. Radiation dose for breast – 38.9 Gy, for axilla – 30 Gy



Fig.5. Operative wound after partial breast resection with axillary lymph nodes dissection L-I/II



Fig.6. After 4 years follow-up

Complications

There were no serious local postoperative wound complications. The seromas around the area of the operating suture were removed by aspiration punctures under ultrasound control. As usual, axillary lymphoedema lasted 1–1.5 months. The grade 1–2 arm lymphedema occur in 3 (8%) pts. Slight breast edema and grade 1 radiodermatitis was observed in half of the patients. Reoperation due to a local recurrence in postoperative scar was done in two cases (5.5%). 4 (11%) patients died 2–4 years after surgery due to metastatic lesions to the brain, lungs, and liver. Therefore 5-years overall survival rate was 89 %.

The cosmetic appearance of the breast was evaluated by the patients as good and satisfactory a few months after surgery (fig. 3, 6).

Our experience shows that the combination of chemotherapy and radiation therapy in the neoadjuvant mode significantly affects the primary tumor and regional lymph nodes, which allows us to consider the possibility of organ-saving operations in patients with breast cancer. Direct irradiation to a malignant tumor as a method of targeted preoperative radiation therapy is more appropriate in our opinion than breast irradiation in the postoperative period.

Conclusions

Irradiation of malignant tumor in breast should be considered as a rational component in the combined preoperative treatment of breast cancer patients.

Breast conservative surgery can be safely performed after neo-adjuvant chemo- and radiation therapy. Oncoplastic surgery should be planned after receiving positive dynamics of reduction of tumor mass in the breast.

Preoperative radiotherapy of breast cancer is safe and does not impact significantly on perioperative complications.

Resumo

Mamo-konservada kirurgio (MKK) sekve de adjuvanta radioterapio (RT) kaj kemioterapio estas konsiderata kiel la preferata kuracmetodo en la pacientoj (ptoj) kun I-II stadioj de mama kancero [1]. Se radiado estas efika kontraŭkancera kuracrimedo, kial ĝi uzis post forigo de mama kancero?

Celo: analizi la rezultojn de MKK en la mamkanceraj malsanuloj kiuj havis la antaŭoperacian kemio-radiokuracadon.

Metodoj: En la retrospektiva studo estis 36 virinoj kun mamo-kancero de stadioj T1 (19 ptoj) kaj T2 (18 ptoj). Molekulaj subtipoj: luminal A – 16 ptoj, luminal B – 5, HER2-neu – 8, triobla negativo – 7 ptoj. Skemo de la kuracado: antaŭoperacia radiada- aŭ kemio-radiada terapio, MKK kun aksela limfonodektomio, postoperacia radiada- / kemia- / hormona terapio dependis de tumora histologio, aĝo, hormona statuso, kaj risko-faktoroj. RT (Terabalt-100, Co-60): antaŭoperacia mama radiado 30–35 Gy / 2.6–2.9 Gy por ĉiutaga frakcio aŭ 5 Gy por frakcio × 5 tagoj. Rezultoj. Ne estis gravaj postoperaciaj vundaj komplikacioj. La grado 1–2 braka limfedemo okazis en 3 (8%) ptoj. Malpeza mama edemo kaj grado 1 radiodermatito estis observitaj en la duono de la ptoj. Kosmetika aspekto de la mamoj estis bona kaj kontentiga kelkajn monatojn post la kirurgio. Reoperacio pro loka recidivo estis farita en du kazoj (5,5%). 4 (11%) ptoj mortis 2–4 jarojn post kirurgio pro metastaza malsano. La 5-jara de postvivanta rango estis 89%.

Konkludoj: MKK povas esti efektivigita sekure post la antaŭoperacia kemioterapio kaj radioterapio. Antaŭoperacia RT de mama kancero estas sekura kaj ne influas signife sur la postoperaciaj vundaj komplikacioj.

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