



EARLY BREAST CANCER: SURGERY AND RADIOTHERAPY

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Comparison of survival outcomes in young patients with breast cancer receiving contralateral prophylactic mastectomy versus unilateral mastectomy

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Background: Contralateral prophylactic mastectomy (CPM) has been performed for several decades in patients with unilateral breast cancer (BC). However, the survival benefits of CPM are controversial, particularly in young women.

Methods: The clinical data of 69,000 young female patients (age \leq 40 years) who were diagnosed to have unilateral BC and underwent UM or CPM between January 1, 2000 and December 31, 2019 were retrieved from the Surveillance, Epidemiology, and End Results (SEER) database. The following patients were excluded from the final analysis: age > 40 years, male, those with unconfirmed pathological diagnosis, those with bilateral BC, those lacking SEER cause-specific death classification, those lacking months of survival data, and those with uncertainty regarding UM or CPM.Propensity score matching (PSM) was performed between the CPM and UM groups. The overall survival (OS) rate and BC-specific survival (BCSS) rate were determined for both groups.

Results: A total of 36528 patients (21600 and 14928 patients in the UM and CPM groups, respectively) were included in this study. The mean (SD) age of follow-up was 35.5 (4.0) years. The relative rate of CPM increased from 12.3% in 2000 to 55.7% in 2013 and then gradually decreased to 47.4% in 2019. After PSM, 13089 patients remained in each group. The CPM group showed a higher 5-year OS rate (82.1% vs. 75.8%) and a higher 5-year BCSS rate (83.5% vs. 77.7%) than the UM group. Multivariate Cox proportional hazards regression analysis showed that CPM significantly decreased 25% risk of all-cause mortality (OS, hazard ratio [HR]: 0.75, 95% confidence interval [CI]: 0.70–0.80, P < 0.001) and 25% risk of BC-specific mortality (BCSS, HR: 0.75, 95% CI: 0.70–0.80; P < 0.001) in young BC patients as compared to UM. Almost consistent results were observed in subgroup analyses based on different TNM stages, molecular subtypes, race, tumor grade, marital status, radiotherapy status, and chemotherapy status, except for some.

Conclusions: This study suggests that CPM improved OS and BCSS benefits in young BC patients as compared to UM. Randomized clinical trials with a larger sample size are required in the future to confirm these results.

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The impact of the extent of the type of primary breast cancer (BC) surgery from the analysis of historical Italian trials

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Background: Breast-conserving surgery (BCS) is the treatment of choice for women with early-stage BC. Several studies indicated a better outcome in patients undergoing BCS plus radiotherapy (RT) in comparison with mastectomy (MAST) +/- RT (PMID:33950173, 27344114). Indeed, in comparison with MAST, BCS reduces the extent of surgery, but the addition of radiotherapy (RT) makes it hard to understand whether the differences in outcome may be attributed to the extent of the surgery only.

Methods: We performed a competing risks re-analysis in terms of dynamics and crude cumulative incidence (CCI), of distant recurrence free survival (DRFS) from two historical randomized clinical trials which of the Istituto Nazionale dei Tumori of Milan: the "Milan 1" trial (n=701; 1973-1980, PMID:7015141) which compared MAST with BCS plus RT (BCS+RT) and the "Milan 3" trial (n=567; 1987-1989, PMID:

8387637) which adopted the same surgical conservative approach with (BCS +RT) or without (BCS -RT) RT. Clinical features such as primary tumour size, axillary lymph node status (N) and menopausal status were considered.

Results: Concerning distant recurrence (DR) dynamics in Milan 1 trial, evidence of a different intensity of cause-specific hazard was found among subgroups related to surgery and lymph-node status (test of interaction effect: P=0.005), though with similar multi-peaked hazard patterns. Indeed, we observed that a MAST-related worse outcome is present in women with positive N (N+). Analysis of CCI reveals that, for the subgroup of N+ patients in Milan 3 trial, removal of RT from BCS (BCS -RT) results in 30% higher incidence of DR, comparable to the difference between MAST N+ and BCS+RT N+ patients in the Milan 1 trial.

Conclusions: In this re-analysis of historical randomized clinical trials, we report that the worse outcome of MAST in comparison with BCS may be mainly attributed to higher extensive surgery and that the effect of the extent of the surgery without RT is mostly confined to patients with N+ BC. The effect of RT, as assessed by the reanalysis of Milan 3 trial, is likely related to a combined effect of the control of local recurrences, and the potential systemic effect of RT.

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Malignant phyllodes tumor: Survival outcome of different surgical approaches

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Background: Malignant phyllodes tumor is a subtype of fibroadenomas but with invasive behaviors that accounts for 1% of all breast cancers. About one in every 4 phyllode tumors is malignant. The available treatment modalities for malignant phyllode tumors are wide excision or mastectomy with adjuvant radiotherapy and in case of distant metastasis, adjuvant chemotherapy is added. However, Due to its scarcity, there are no enough data about the best treatment modality and that is the what our study aims to find.

Methods: We extracted the data of 1971 female patients from Surveillance, Epidemiological, and End Results (SEER) database. All of them had Malignant Phyllode tumor. We divided the patients into 3 groups; Conservative surgery, simple mastectomy, and radical mastectomy. For each group we further subdivided them into 3 more groups, surgery with no systemic therapy, adjuvant radiotherapy, and adjuvant chemotherapy. For each subgroup, we measured the relative 5-year survival. We also performed Kaplan-Meier curve and log rank test using SPSS 25 for survival analysis.

Results: The 5-year relative survival of conservative surgery, simple mastectomy and radical mastectomy were (98.1%, 86.2%, 77.5% respectively; P<0.001). With sub stratification of the 3 available surgeries, we compared the 5 year-relative survival of adjuvant therapy with each group; adjuvant radiotherapy with conservative surgery, simple mastectomy and radical mastectomy were (94.9%, 83.2%, 64.7% respectively; P<0.001) and for Adjuvant chemotherapy, they were (50.8%, 66.4%, 22.1% respectively; P<0.001).

Conclusions: The results of this study highlight that conservative surgery with no adjuvant therapy to be the treatment modality of choice as it has the best survival outcome. However, If the tumor is abnormally large, simple mastectomy is recommended instead. Regarding adjuvant therapy, Adjuvant radiotherapy shows better survival than adjuvant chemotherapy but both shows no survival benefit compared to surgery. So, we recommend that adjuvant radiotherapy to be cautiously used with selective patients. Additionally, adjuvant chemotherapy should be avoided to avoid unnecessary side effects.

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