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Prognosis after treatment for loco-regional recurrence in 535 high-risk breast cancer patients from the DBCG 82 b&c randomization studies

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Background and aim: In the DBCG 82 b&c trials 3083 patients with stage II and III breast cancer were randomized to ± postmastectomy RT. The aim of the present study was to investigate the prognosis after loco-regional recurrence (LRR) and to compare different types of salvage treatment.
Material and methods: A total of 535 patients from the DBCG 82 b&c trials experienced a LRR a first and only site of failure. LRR was defined as recurrence on the chest wall, axillary or supra/infraclavicular regions without concomitant distant metastases (DM). Follow-up data were selected from medical records and general practitioners. Endpoints were overall survival and DM. The different type of salvage treatments were compared in terms of their ability to achieving complete remission and persistent loco-regional control of the LRR.
Results: Complete remission of the LRR depended on type of salvage treatment and was 96% among patients having surgery+RT (176/183), 93% among patients having surgery alone (139/149), 81% among patients having RT alone (88/109) and 46% among patients having systemic treatment alone (37/80). Persistent loco-regional control was 58% among patients having surgery+RT (107/183), 32% among patients having surgery alone (47/149), 49% among patients having RT alone (53/109) and finally 25% among patients having systemic treatment alone (20/80).
The 5-, 10- and 15-year survival after LRR was 36%, 20% and 14%, respectively. The 5-, 10- and 15-year actuarial probability of DM was 73%, 81% and 84%, respectively. In univariate analysis, original randomization group was not important for survival (p = 0.15), whereas site of LRR (p < 0.001), time interval to LRR (p < 0.001) and the following original tumor variables: tumor size (p = 0.001), malignancy grade (p = 0.002), invasion of the skin (p = 0.02), invasion of the fascia (p = 0.01), number of positive nodes (p < 0.001) and extracapsular invasion (p = 0.001) were prognostic factors for survival. In multivariate analysis small primary tumor size (p = 0.01), chest wall or axillary failure alone (p < 0.001) and long interval to LRR > 2 years (p < 0.001) were independent good prognostic factors for survival.
Conclusion: Persistent loco-regional control was increased among patients having surgery and RT as salvage treatment after LRR. Survival after treatment for LRR was poor, but with independent good prognostic factors for survival being small primary tumor, location of the LRR at the chest wall or in the axilla and a long time interval from mastectomy to LRR of more than 2 years.
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Long-term risk of cardiovascular disease in 10-year survivors of breast cancer

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Purpose: To assess cardiac risk according to radiation field in breast cancer patients, accounting for cardiac risk factors.
Patients and methods: We studied incidence of cardiovascular disease (CVD) in a group of 10-year survivors (n = 4368) who were treated in the NKI and the DDHK for early breast cancer between 1970 and 1987. Follow-up was for 98% complete until January 2000. Treatment-specific incidence of CVD was evaluated by calculating standardized incidence ratios (SIRs) based on comparison with general population rates and by using Cox proportional hazards regression.
Results: After a median follow-up of 18 years 942 cardiovascular events (acute myocardial infarction (MI), angina pectoris and congestive heart failure) were observed resulting in a SIR of 1.3 (95%CI: 1.2−1.4) and an absolute excess risk of 63/10,000 person-years. For the treatment period 1970−79, radiotherapy (RT) on the internal mammary chain (IMC) was associated with an increased risk of MI both for patients wit left- and right-sided tumors in comparison with non-irradiated patients; hazard ratio (HR), 2.2; 95%CI: 1.3−3.7, and 2.9; 95%CI: 1.7−5.1, respectively, while for the treatment period 1980−86, these risks had declined to 0.8 (0.4−1.6) and 0.9 (0.5−1.7), respectively. Patients irradiated on the left chest wall experienced a significantly increased risk of MI as compared to those

treated with surgery only in both treatment periods (HR, 2.8; 95%CI: 1.4−5.5, and 3.7; 95%CI: 1.2−11.5, respectively). RT on the right chest wall showed a non-significantly 1.5-fold increased risk of MI for the period 1970−79, while from 1980 on, no MIs occurred in this treatment group. RT on the breast only, applied from 1980 on, was not associated with an increased risk of MI, with HRs of 0.7 (95%CI: 0.3−1.6) for left-sided, and 0.9 (95%CI: 0.4−2.2) for right-sided tumors. Hypertension, smoking, diabetes mellitus and hypercholesterolemia acted as independent risk factors for MI, with HRs of 2.0 (1.5−2.7), 2.1 (1.5−2.7), 1.3 (0.9−1.8) and 3.0 (2.2−4.1), respectively. Analysis on the combined effects of smoking and RT revealed a more than additive effect on MI, with a HR of 3.0; 95%CI: 2.0−4.5 (HR for irradiated non-smokers, 1.3; HR for non-irradiated smokers, 1.4).
Conclusions: Radiotherapy after 1979 is not associated with increased MI risk, with the only exception for radiation to the left chest wall. The combination of smoking and RT appears to exert a greater than additive effect on MI risk.

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Lymph node ratio as prognostic factor in node-positive breast cancer

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Background: The latest AJCC/TNM Cancer Staging 6th edition introduced over previous editions major changes in the pathologic nodal (pN) staging that more accurately reflect breast cancer disease continuum. However, concerns have been expressed regarding stage migration, i.e. decreased separation between prognostic groups due to reclassification. Some authors have suggested the lymph node ratio (LNR), defined as the proportion of involved nodes among excised nodes, as a potential alternative. But, before the LNR can be considered for staging, many issues must be settled. Studies of the LNR have been based on relatively homogeneous single institution data, or on large population data but with restrictive selection and using complex multivariate models. The present study will address how the LNR performs, without adjustment, in heterogeneous cases.
Material and Methods: Data for women diagnosed in 1988−97 with primary invasive node-positive breast carcinoma were abstracted from the Surveillance, Epidemiology, and End Results 9-registries (SEER 2004). Other than required histology confirmation (pathologic staging), there were no restrictions based on tumour size, age, or treatment. Cases with biopsy only and as few as one node examined were eligible. Three LNR groups were defined: low LNR (≤ 0.25), intermediate LNR (0.25−0.75), and high LNR (> 0.75). Classification performance was evaluated by the survival separation between prognostic groups, as compared with the TNM pN categories. The LNR and the TNM pN were examined within cases previously staged according to the AJCC 3rd edition. Survival estimates used the Kaplan-Meier method. Event was death from any-cause. Significance testing used the logrank test, larger values of Chi^2 indicating better separation.
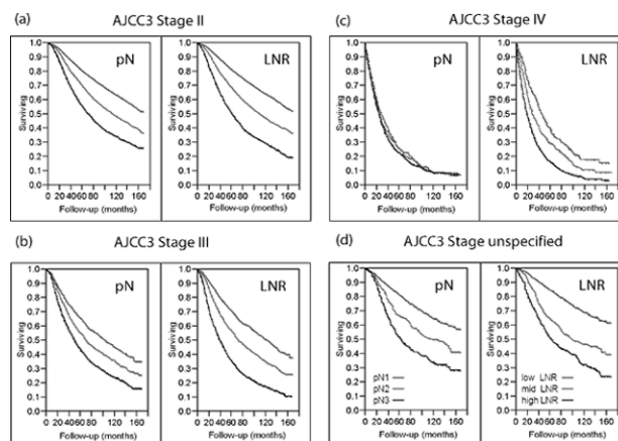

Fig. 1: Overall survival in node-positive breast cancer. Nodal classification based on the 6th TNM (pN) compared with classification based on Lymph node ratio (LNR), applied to cases already previously staged according to the 3th AJCC TNM system (AJCC3).