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Breast Cancer Therapy-Related Cardiac Dysfunction Identifying in Kazakhstan: Preliminary Findings of the Cohort Study

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Abstract : Cardiotoxicity associated with anticancer treatment, now defined as cancer therapy-related cardiac dysfunction (CTRCD), accompanies cancer patients and negatively impacts their survivorship. Currently, a cardio-oncological service is being created in Kazakhstan based on the provisions of the European Society of Cardio-oncology (ESC) Guidelines. In the frames of a pilot project, a cohort study on CTRCD conditions was initiated at the Aktobe Cancer center. One hundred twenty-eight newly diagnosed breast cancer patients started on doxorubicin and/or trastuzumab were recruited. Echocardiography with global longitudinal strain (GLS) assessment, biomarkers panel (cardiac troponin (cTnI), brain natriuretic peptide (BNP), myeloperoxidase (MPO), galectin-3 (Gal-3), D-dimers, C-reactive protein (CRP)), and other tests were performed at baseline and every three months. Patients were stratified by the cardiovascular risks according to the ESC recommendations and allocated into the risk groups during the pre-treatment visit. Of them, 10 (7.8%) patients were assigned to the high-risk group, 48 (37.5%) to the medium-risk group, and 70 (54.7%) to the low-risk group, respectively. High-risk patients have been receiving their cardioprotective treatment from the outset. Patients were also divided by treatment - in the anthracycline-based 83 (64.8%), in trastuzumab- only 13 (10.2%), and in the mixed anthracycline/trastuzumab group 32 individuals (25%), respectively. Mild symptomatic CTRCD was revealed and treated in 2 (1.6%) participants, and a mild asymptomatic variant in 26 (20.5%). Mild asymptomatic conditions are defined as left ventricular ejection fraction (LVEF) ≥50% and further relative reduction in GLS by >15% from baseline and/or a further rise in cardiac biomarkers. The listed biomarkers were assessed longitudinally in repeated-measures linear regression models during 12 months of observation. The associations between changes in biomarkers and CTRCD and between changes in biomarkers and LVEF were evaluated. Analysis by risk groups revealed statistically significant differences in baseline LVEF scores (p 0.001), BNP (p 0.0075), and Gal-3 (p 0.0073). Treatment groups found no statistically significant differences at baseline. After 12 months of follow-up, only LVEF values showed a statistically significant difference by risk groups (p 0.0011). When assessing the temporal changes in the studied parameters for all treatment groups, there were statistically significant changes from visit to visit for LVEF (p 0.003); GLS (p 0.0001); BNP (p<0.00001); MPO (p<0.0001); and Gal-3 (p<0.0001). No moderate or strong correlations were found between the biomarkers values and LVEF, between biomarkers and GLS. Between the biomarkers themselves, a moderate, close to strong correlation was established between cTnI and D-dimer (r 0.65, p<0.05). The dose-dependent effect of anthracyclines has been confirmed: the summary dose has a moderate negative impact on GLS values: -r 0.31 for all treatment groups (p<0.05). The present study found myeloperoxidase as a promising biomarker of cardiac dysfunction in the mixed anthracycline/trastuzumab treatment group. The hazard of CTRCD increased by 24% (HR 1.21; 95% CI 1.01;1.73) per doubling in baseline MPO value (p 0.041). Increases in BNP were also associated with CTRCD (HR per doubling, 1.22; 95% CI 1.12;1.69). No cases of chemotherapy discontinuation due to cardiotoxic complications have been recorded. Further observations are needed to gain insight into the ability of biomarkers to predict CTRCD onset.

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