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Cardiac biomarkers for the prediction of cardiotoxicity in cancer patients: a meta-analysis

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Background: Cancer therapy-related heart failure is the most concerning cardiac adverse event in patients undergoing cancer therapy. Valid diagnostic measures are fundamental for a timely diagnosis but systematic data on the use of diagnostic parameters in this collective is sparse. Cardiac biomarkers may be beneficial for diagnosis and screening of cancer therapy-related heart failure.

Purpose: Systematic data for cardiac biomarkers in cancer therapy-related cardiotoxicity is urgently needed to establish guideline recommendations. We therefore conducted the present systematic review and meta-analysis to assess cardiac troponin and (N-terminal pro) brain natriuretic peptide (BNP/NT-proBNP) in the prediction of left ventricular (LV) systolic dysfunction in cancer patients.

Methods: Cochrane, PubMed, Web of Science, and Wiley Library were screened for studies investigating cardiac troponin or BNP/NT-proBNP in cancer patients receiving cytotoxic chemotherapy with and without anthracyclines, human epidermal growth factor receptor 2 (HER2) inhibitor therapy and radiotherapy. Reduced LV ejection fraction (LVEF) was defined as primary endpoint.

Results: A total of 5772 patients from 58 studies were included. Chemotherapy and HER2 inhibitor therapy was associated with an elevation of troponin levels above the 99th percentile (odds ratio (OR) = 14.3; 95% confidence interval (CI): 6.9-29.5). Patients treated with anthracyclines and high-dose chemotherapy had the highest rates of troponin elevation (OR = 17.5; 95% CI: 10.1-30.2 for anthracyclines; OR = 75.1; 95% CI: 4.4-1296.9 for high-dose chemotherapy, respectively). The risk for LVEF impairment was increased in troponin positive patients compared to troponin negative patients under high-dose regimens (OR = 97.9; 95% CI: 52.1-183.8) and anthracyclines with and without concomitant HER2 inhibitors (OR = 7.0; 95% CI: 1.4-34.1 and OR = 10.5; 95% CI: 2.0-54.3). Cardiac troponin below the 99th percentile had a negative predictive value of 94% for the prediction of cardiotoxicity. Absolute plasma BNP/NT-proBNP was increased in patients with LV dysfunction (standardized mean difference = 0.6; 95% CI = 0.0-1.2) but pathologically increased BNP/NT-proBNP did not predict decreased LVEF (OR = 2.0; 95% CI: 0.9-7.2). Preventive β-blocker therapy and angiotensin converting enzyme (ACE) inhibitor therapy was associated with decreased troponin elevation compared to control (OR = 2.9; 95% CI: 1.1-7.3; Figure 4). The effect was more pronounced in ACE inhibitor-treated patients compared to β-blocker-treated patients (Chi² = 4.4; p = 0.04; I² = 77.4%).

Conclusion: Elevated troponin levels predict left ventricular dysfunction in cancer patients and a decrease in troponin may indicate response to cardioprotective therapy in cancer therapy-related cardiotoxicity. Cardiac troponin qualifies as a screening test to identify patients at high risk for manifest cardiotoxicity who require referral to cardio-oncology units.