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Cardiac biomarkers for the detection of anthracycline cardiotoxicity in childhood cancer - a meta-analysis

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Introduction: Heart failure is the most concerning cardiovascular side effect of anthracycline chemotherapy. Pediatric cancer patients and survivors of childhood cancer are particularly vulnerable to cancer therapy-related cardiotoxicity. Cardiac biomarkers may be beneficial for screening and diagnosis of anthracycline-related heart failure in pediatric cancer patients and survivors of childhood cancer but systematic data is not yet available.

Purpose: To evaluate (N-terminal pro) brain natriuretic peptide (BNP/NT-proBNP) and cardiac troponin for screening and prediction of cancer therapy-related cardiotoxicity in pediatric cancer patients and survivors of childhood cancer.

Methods: Cochrane, PubMed, Web of Science, and Wiley Library were screened for studies investigating cardiac troponin or BNP/NT-proBNP in pediatric cancer patients receiving anthracycline therapy or survivors of childhood cancer. The primary endpoint was left ventricular (LV) dysfunction as defined by decreased ejection fraction (EF) or fractional shortening (FS). The study was registered at the International prospective register of systematic reviews (PROSPERO) (CRD42018106616).

Results: A total of 1643 subjects from 27 studies were included. BNP/NT-proBNP levels were higher in patients post-treatment compared to control subjects or pre-treatment values (standardized mean difference = 1.0; 95% CI = 0.6-1.4; n = 239). The risk for left ventricular (LV) dysfunction was increased in patients with elevated BNP/NT-proBNP (OR = 5.5; 95% CI = 2.0-15.2; n = 357). This was demonstrated for acute cardiotoxicity (OR = 22.3; 95% CI = 3.3-151.1; n = 88) and in survivors of childhood cancer (OR = 3.2; 95% CI = 1.0-10.0; n = 269). Sensitivity for the prediction of acute or subacute LV dysfunction was 28.9% and specificity was at 91.7%. The frequency of troponin elevations was increased after anthracycline therapy (Odds ratio (OR) = 3.6; 95% confidence interval (CI) = 2.0-6.5; n = 305) but troponin was not associated with LV dysfunction (OR = 0.2; 95% CI = -0.2-0.5; n = 273).

Conclusion: BNP/NT-proBNP is elevated in pediatric patients receiving anthracycline chemotherapy and serves as a marker for the prediction of cardiotoxicity and screening for late cardiotoxicity in survivors of childhood cancer. So far, there is no systematic evidence on a benefit of cardiac troponin for the detection of anthracycline cardiotoxicity in children. Standardized recommendations on the role of cardiac biomarkers are needed for the optimal detection of anthracycline cardiotoxicity in childhood cancer patients.