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Risk factors for heart failure after doxorubicin chemotherapy for breast- or colorectal cancer

Abstract: 1958

Risk factors for heart failure after doxorubicin chemotherapy for breast- or colorectal cancer

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Background: Development of dilated cardiomyopathy (DCM) after anthracycline chemotherapy is mainly influenced by anthracycline cumulative dose. Based on published data, doxorubicin treatment under cumulative dose of 450 mg/m^2 is considered to be associated with a low incidence of heart failure (HF). Patients older than 65 years are more susceptible for anthracycline-related DCM. Risk factors for development of HF after anthracycline treatment is still not known in details. Dexrazoxane may have a protective effect against cardiotoxicity, but its role remained equivocal.

Purpose: Our purpose was to assess the incidence of HF after doxorubicin therapy and to identify the risk factors for HF.

Methods: With use of the anonymized financial database of the Hungarian National Health Insurance Company we performed a retrospective nation-wide study. Study subjects and outcome events were defined with the International Classification of Diseases (ICD) codes. We enrolled all the patients who had histological confirmation for breast- or colorectal carcinoma between 1st January 2004 and 31st December 2015. 164 640 patients met these inclusion criteria. We excluded the subjects who did not have a minimum 3-year long preceding period documented without any chemotherapy, or assignment of I50 (HF) and I420 (DCM) ICD codes before index chemotherapy. HF outcome event was defined by assignment of I50 ICD code at hospital discharge, or in autopsy report. HF event incidence was only analysed at the subjects with at least 3-year follow-up data or reaching the event earlier. We used multivariate binary stepwise logistic regression to calculate odds ratios (OR) for HF. Oncology state was considered as potential confounding factor.

Results: 3298 doxorubicin-treated patients were eligible for HF analysis. We found 6.2% cumulative incidence for HF. Incidence was essentially influenced by doxorubicin cumulative dose and age. Doxorubicin cumulative dose over 300 mg/m^2 was proven independent predictor for HF (for dose 301–400 mg/m^2 OR: 1.40, p=0.083, for dose over 400 mg/m^2 OR: 2.29, p=0.008). Risk of HF was elevated with older age: OR for HF at age 50–59 was 2.95, at age 60–69 was 4.02 and at age over 70 was 5.69, compared to those under 40. No other chemotherapy, besides doxorubicin, was found to have cumulative dose-dependent effect on HF. Diabetes mellitus (OR: 1.47), capecitabine (OR: 2.47), 5-fluorouracil (OR: 1.43), bevacizumab (OR: 2.41) and carboplatin (OR: 1.88) were also proven

independent variables with significant association with HF (p values <0.05). Presence of trastuzumab, taxanes, cyclophosphamide and dexrazoxane had no significant impact on the HF outcome event.

Conclusion: We found significant elevation of HF incidence with increasing age, even over 50 years and with doxorubicin cumulative dose over 300 mg/m^2. Completing the treatment with pyrimidine-analogues, platinum-containing drug (carboplatin) and bevacizumab was associated with higher risk for HF.