

Risk Factors for Heart Failure after Doxorubicin Chemotherapy for Breast or Colorectal Cancer

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Aims and Methods

- Aims: to assess the incidence of HF after doxorubicin therapy and to identify the risk factors for HF.
- Retrospective study: anonymized **financial database** of the Hungarian National Health Insurance Company.
- Subjects: **breast or colorectal cancer with histology** between January 2004 - December 2015, treated **with doxorubicin**.
- Enrolment criteria:
 - a min. 3-year preceding period w/o any chemotherapy or HF and DCM ICD-10* codes (I50, I420)
 - no other anthracycline applied
- HF outcome analysis:
 - HF ICD-10 code (I50) at hospital discharge or in autopsy report (except immediate cause of death)
 - only at the subjects with at least 3-year F-U data or reaching the HF event earlier
 - multivariate binary stepwise logistic regression to calculate OR for HF (IBM SPSS Stat. ver. 23)

*World Health Organization. (1992). International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Geneva

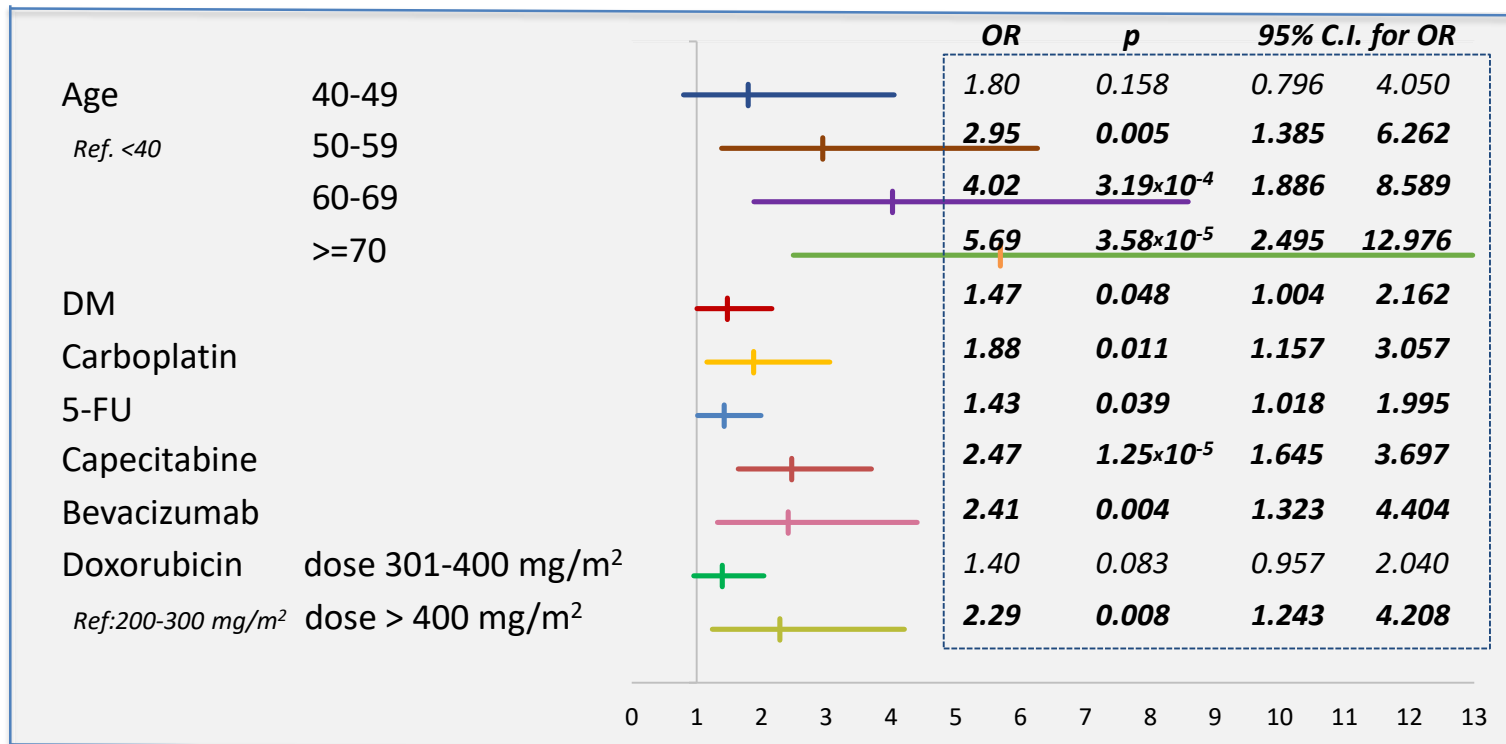
Clinical characteristics, N=3298

Characteristics	N	%	Characteristics	N	%
<i>Age category, year</i>			<i>Cancer Stage</i>		
<40	347	10.5	No spread or invasion	859	26.0
40–49	695	21.1	Regional lymph node or nearby structure invasion	1026	31.1
50–59	1153	34.9	Distant lymph node or other distant metastasis	576	17.5
60–69	844	25.6	Missing data	837	25.4
70+	259	7.9			
<i>Gender</i>			<i>Pre-existing cardiovascular conditions and risk factors</i>		
Male	25	0.8	Diabetes mellitus	399	12.1
Female	3273	99.2	Hypertension	1921	58.3
<i>Cancer localization</i>			Hyperlipidemia	491	14.9
Breast	3288	99.7	Angina pectoris	689	20.9
Colorectal	10	0.3	Previous MI or coronary revascularization	67	2.0

Cancer therapy	N	%
Radiation	2785	84.4
Doxorubicin cumulative dose, mg/m ²		
200-300	2678	81.2
301-400	523	15.9
400+	97	2.9
Taxanes		
Paclitaxel	753	22.8
Docetaxel	1835	55.6
Cyclophosphamide	2990	90.6

Cancer therapy	N	%
Pyrimidine-analogues		
Capecitabine	282	8.5
5-fluorouracil	746	22.6
Carboplatin	188	5.7
Targeted therapies (antibodies)		
Trastuzumab	710	21.5
Bevacizumab	97	2.9
Protective agents		
Dexrazoxane	194	5.9

Result of the regression analysis



Summary

- Overall 3-8 year cumulative HF incidence: 6.2%.
- Cumulative dose dependency found only at doxorubicin.
- Significant HF risk elevation over 400 mg/m² doxorubicin cumulative dose.
- The older the age, the higher the risk for HF over 50 years. Main risk factor.
- Significant risk elevation with pyrimidine-analogues, platinum-containing drug (carboplatin), bevacizumab (hypertensive effect?) and with diabetes.
- No long-term HF risk elevation found with trastuzumab (reversible adverse effect) and taxanes.
- No lower HF risk found with dexrazoxane (selection bias?)
- Chest radiation therapy did not increase the risk of HF.
- Despite being a financial data analysis, correlation with the results of published smaller clinical studies* (the same cumulative threshold dose: 400-450 mg/m²).

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*Swain SM, Whaley FS, Ewer MS. Congestive heart failure in patients treated with doxorubicin: a retrospective analysis of three trials. Cancer. 2003;97:2869-79. doi: 10.1002/cncr.11407.