



UKE Paper of the Month May 2016

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A Comprehensive Multistate Model Analyzing Associations of Various Risk Factors With the Course of Breast Cancer in a Population-Based Cohort of Breast Cancer Cases

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ABSTRACT: We employed a semi-Markov multistate model for the simultaneous analysis of various endpoints describing the course of breast cancer. Results were compared with those from standard analyses using a Cox proportional hazards model. We included 3,012 patients with invasive breast cancer newly diagnosed between 2001 and 2005 who were recruited in Germany for a population-based study, the Mamma Carcinoma Risk Factor Investigation (MARIE Study), and prospectively followed up until the end of 2009. Locoregional recurrence and distant metastasis were included as intermediate states, and deaths from breast cancer, secondary cancer, and other causes were included as competing absorbing states. Tumor characteristics were significantly associated with all breast cancer-related endpoints. Nodal involvement was significantly related to local recurrence but more strongly related to distant metastases. Smoking was significantly associated with mortality from second cancers and other causes, whereas menopausal hormone use was significantly associated with reduced distant metastasis and death from causes other than cancer. The presence of cardiovascular disease at diagnosis was solely associated with mortality from other causes. Compared with separate Cox models, multistate models allow for dissection of prognostic factors and intermediate events in the analysis of cause-specific mortality and can yield new insights into disease progression and associated pathways.

STATEMENT: *This work enables new insights into breast cancer epidemiology and associative pathways. The statistical technique of multistate modelling allows the analysis of multiple important cornerstones of disease-progression, for example local and distant metastases, simultaneously. In this work, the prognostic impact of tumor characteristics as well as lifestyle factors on the course of breast cancer were analyzed for the first time.*



BACKGROUND: This work was performed as a cooperation between the Department for Medical Biometry and Epidemiology and the Department of Cancer Epidemiology / Clinical Cancer Registry at UKE, and with the Division of Cancer Epidemiology of the German Cancer Research Center (DKFZ) in Heidelberg. The work was partially funded by Deutsche Krebshilfe e.V. (grants 70-2892-BR I, 108253, and 108419). The authors have strong research interests in statistical methods for cancer epidemiology and prognostic pathways in cancer epidemiology.