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## **Long-term survival of female breast cancer patients in Germany - results from a population-based high resolution study from Saarland**

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Breast cancer (BRC) is the most frequent invasive cancer among women worldwide, with estimated 421,000 new cases and 129,000 deaths in Europe in 2008. Mammography screening and advances in treatment are considered as main reasons for the observed decline in BRC mortality in developed countries during the past two decades. Up to now, population-based data on BRC survival were commonly restricted to age- and stage-specific estimates. This dissertation aims at extending these data and provides up-to-date survival of BRC patients from Germany by age, stage and further tumor characteristics, data on the delivery of cancer care and survival according to major treatment options of clinical practice guidelines (CPG). It further compares most recent survival of BRC patients and preceding trends from Germany and the US.

For this work, data from the population-based Saarland Cancer Registry were used and included female patients diagnosed with invasive BRC and followed up between 1989 and 2009. Period analysis methodology and regression modeling were used to obtain estimates of 5-year relative survival (RS) and relative excess risk (RER) of death as a measure of cancer related excess mortality. Provision of cancer care according to major recommended treatment options was presented by age and over time. For a comparison with the US, additional data from the Surveillance, Epidemiology, and End Results Program were utilized.

In 2005–2009, overall age standardized 5-year RS was 83%, ranging from 89% for patients aged 15–49 years to 77% for patients aged  $\geq 70$  years. Age standardized 5-year RS was 98%, 80% and 22% for patients with localized, locally or regionally advanced and metastasized BRC, respectively. Detailed analyses consistently revealed lower survival of patients with high grade, hormone receptor (HR) negative or HER2/neu positive tumors and of elderly BRC patients.

The analyses demonstrated increasing adherence to CPG between 2000 and 2009 (e. g. rises in the usage of breast conserving surgery (BCS) given to 67% of the patients in 2008/09, or chemotherapy and antiestrogen treatment provided to 79% and 93% of the patients with nodal positive or HR negative BRC and HR positive or mixed BRC in 2008/09, respectively) and the advent of SND for staging and use of trastuzumab in BRC patients with HER2/neu positive tumors (increases from 1% in 2000/01 to 62% and 47% in 2008/09, respectively). The analyses further demonstrated major disparities in the provision of cancer treatment by age (e. g. chemotherapy given to 91% of patients with nodal positive or HR negative tumors aged 15–69 years compared to only 40% of such patients aged  $\geq 70$  years).

Patients with localized T1/T2 tumors receiving a BCS followed by adjuvant radiotherapy or mastectomy alone had a 5-year RS of 100%, and 5-year RS of patients with T3/T4 tumors with positive lymph nodes who received mastectomy and

radiotherapy was 74%. Patients with nodal positive and HR negative BRC who were not treated with chemotherapy had a 5-year RS of 29% (RER 2.89, 95% CI 1.46–5.71) compared to 54% for patients obtaining chemotherapy. Patients with HR positive or mixed tumors without antiestrogen treatment had a 5-year RS of 86% (1.75, 0.99–3.07) compared to 97% if such treatment was given.

Between 1993 and 2008, age standardized 5-year RS has steadily increased in Germany and the US from 72% and 83% to 83% and 88%, respectively, with most improvement seen for patients with locally or regionally advanced BRC, and to a lesser extent also for patients with localized BRC. Prognosis of patients with metastasized BRC has remained very poor overall, with increases essentially being restricted to younger patients. If adjusted for stage, the differences in 5-year RS between both countries reported in the past had diminished over time and eventually disappeared.

Major strengths of this work include the use of a population-based database with a high level of detail and completeness of information and an almost complete case ascertainment and follow-up of the patients. Saarland is quite representative for Germany and its health care system. The use of period analysis methodology and regression modeling for RS allowed providing up-to-date estimates of RS and to evaluate the effects of tumor characteristics and treatment on BRC survival and cancer related excess mortality. Major limitations arose from the limited size of the Saarland population and hence the study population of BRC patients, which hampered detailed analyses of less frequent clinical types of BRC. Furthermore, the extent of missing information on cancer treatment and missing further treatment details restricted the levels of detail of the analyses that were possible in this work.

This dissertation revealed inferior survival of elderly BRC patients aged 70 years or older compared to younger patients consistently across all clinical subgroups of BRC and even demonstrated an increasing gap in survival between elderly BRC patients and younger ones in Germany during the past two decades. However, elderly BRC patients received recommended treatment less often compared to younger patients. The analyses further revealed tentatively increased cancer related excess mortality among BRC patients who did not receive guideline adherent treatment. This dissertation may thus provide relevant evidence of the effect of adherence to CPG on cancer survival on a population level and demonstrated striking survival deficits observed for elderly BRC patients, who today represent one out of three patients with a newly diagnosed BRC.