Metabolic pathways, body constitution, and tumor characteristics in relation to breast cancer prognosis

PhD thesis - Half time review seminar
November 26, 2018
Conference room, Kamprad, at 1 PM
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Background

Due to improvements in breast cancer diagnostics and treatments, survival has improved leading to a growing number of survivors. The worldwide obesity epidemic influences risk and prognosis. The overall aim is to investigate the combined effect of patient and tumor characteristics on prognosis in different treatment groups, with focus is on body constitution, metabolism, cholesterol, and statins.

Materials and methods

The thesis is based on material from the BCBlood study, a prospective, population-based cohort of primary breast cancer patients who underwent surgery in Lund, Sweden from 2002 to 2012 (n=885; paper I) or 2014 (n=985; paper II and n=1317; paper III). Patients were followed until 2014 (paper I) or 2016 (papers II-III). Body measurements were obtained by research nurses. Data and outcomes were obtained from questionnaires, pathology reports, patient charts and population registries. For papers I and II, tumor-specific expression of HMG-CoA Reductase (HMGCR) was analyzed on tumor tissue microarrays from the cohort. For paper II, genotyping was performed and the ABCB1 3435 (rs1045642) single-nucleotide polymorphism (SNP) was analyzed. Univariable analyzes were performed with LogRank tests and multivariable analyzes with Cox regression proportional hazard models.

Preliminary results

Paper I (published): Moderate and strong expression of HMGCR was associated with less aggressive tumor characteristics compared to weak or no HMGCR expression. HMGCR expression was not associated with disease-free survival.

Paper II (published): Preoperative statin use was not associated with the ABCB1 genotype, HMGCR expression or clinical outcomes. Statin users with the ABCB1 3435 TT-genotype had a borderline increased risk of breast cancer events, higher risk of distant metastasis and shorter overall survival compared to any C-genotypes.

Paper III (in progress): Weight gain in the first postoperative year was associated with a doubled recurrence-risk in patients <50 years. Weight loss was associated with a 3-fold recurrence-risk in patients ≥70 years. Weight changes had no clear association with prognosis in patients aged 50-<70 years.

Significance

Despite advances in treatment, recurrences still affects many breast cancer survivors. Studying host factors such as lipid-associated metabolic factors and statin use may lead to a better risk stratification and new markers for better tailored treatment.
Published papers
