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**Titel des Beitrags:**

Common breast cancer susceptibility alleles are associated with tumour subtypes in BRCA1 and BRCA2 mutation carriers: results from the Consortium of Investigators of Modifiers of BRCA1/2.

**Abstract:**

Previous studies have demonstrated that common breast cancer susceptibility alleles are differentially associated with breast cancer risk for BRCA1 and/or BRCA2 mutation carriers. It is currently unknown how these alleles are associated with different breast cancer subtypes in BRCA1 and BRCA2 mutation carriers defined by estrogen (ER) or progesterone receptor (PR) status of the tumour. We used genotype data on up to 11,421 BRCA1 and 7,080 BRCA2 carriers, of whom 4,310 had been affected with breast cancer and had information on either ER or PR status of the tumour, to assess the associations of 12 loci with breast cancer tumour characteristics. Associations were evaluated using a retrospective cohort approach. The results suggested stronger associations with ER-positive breast cancer than ER-negative for 11 loci in both BRCA1 and BRCA2 carriers. Among BRCA1 carriers, single nucleotide polymorphism (SNP) rs2981582 (FGFR2) exhibited the biggest difference based on ER status (per-allele hazard ratio (HR) for ER-positive = 1.35, 95% CI: 1.17 to 1.56 vs HR = 0.91, 95% CI: 0.85 to 0.98 for ER-negative, P-heterogeneity = 6.5 x 10^-6). In contrast, SNP rs2046210 at 6q25.1 near ESR1 was primarily associated with ER-negative breast cancer risk for both BRCA1 and BRCA2 carriers. The associations of the 12 SNPs with risk for BRCA1 and BRCA2 carriers differ by ER-positive or ER-negative breast cancer status. The apparent differences in SNP associations between BRCA1 and BRCA2 carriers, and non-carriers, may be explicable by differences in the prevalence of tumour subtypes. As more risk modifying variants are identified, incorporating these associations into breast cancer subtype-specific risk models may improve clinical management for mutation carriers.