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# IV.3 The Combined Effects of ERT, Obesity and Tamoxifen Therapy for Breast Cancer on Endometrial Cancer Risk

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TAMOXIFEN, WIDELY used to treat breast cancer, is currently under evaluation as a breast cancer prevention agent in clinical trials. Reports that tamoxifen induces endometrial cancer have raised concern among consumers and practitioners. No prior studies of tamoxifen's effects on endometrial cancer risk have examined the modifying effects of oestrogen replacement therapy (ERT) and obesity. We examined these effects in a matched case–control study of subsequent endometrial cancer following breast cancer conducted within four Surveillance Epidemiology and End Results (SEER) registries (Los Angeles, Iowa, Seattle, and Atlanta cases). The medical histories of 324 case-patients and 671 control-patients were established through the review of medical records and by interview. Tamoxifen use, ERT use and obesity were each statistically significant predictors of endometrial cancer risk. The effect of tamoxifen on endometrial cancer risk was duration related (trend $P=0.001$); relative to non-users, women with more than 5 years exposure to tamoxifen had 3.7-fold greater odds of developing endometrial cancer. Among women with prior ERT exposure, the trend in risk was more pronounced (trend $P<0.0001$) than it was for those with no prior use of ERT (trend $P=0.11$) and this difference was statistically significant (homogenecity $P=0.0001$). The risk of endometrial cancer associated with duration of tamoxifen use also varied by obesity status, with the trend in risk more pronounced among heavier women. Among women above the median body mass index of controls in the study, the odds of endometrial cancer was more than 5-fold greater if the woman had used tamoxifen for more than 5 years; among thinner women, the relative odds of endometrial cancer after more than 5 years of tamoxifen therapy was less than 2. Risk of endometrial cancer associated with tamoxifen therapy was most elevated among those women who previously took ERT and who had high body mass index when diagnosed with breast cancer. These results suggest that both exogenous and endogenous oestrogens substantially modify the effects of tamoxifen on endometrial cancer risk.

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# IV.4 Iatrogenic Risks of Endometrial Carcinoma after Treatment for Breast Cancer in a Large French Case–Control Study

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**In a case–control study, including 135 cases of endometrial carcinoma diagnosed after breast cancer and 467 controls, the relative risks for endometrial carcinoma were higher for women treated with**