RISKS OF SECOND CANCERS AFTER INITIAL TREATMENT AMOMG WOMEN WITH BREAST CANCER.THE OSAKA CANCER REGISTRY DATABASE STUDY

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BACKGROUND and PURPOSE: Breast cancer is the most common cancer among women. The incidence of primary breast cancer has a peak between 40 and 50 years of age among Japanese females. Survival rate of breast cancer in the Japanese population has increased, because diagnostic technique and medical treatment are improved. Most of patients receive some treatments, such as surgical resection, drug therapy or radiotherapy. The acute toxicity of various therapies is well defined. However, the late complications of treatments, including the development of second cancers, are less known. Many breast cancer patients are facing the possibility of developing second cancers. Using the Osaka Cancer Registry database in Japan, we conducted a retrospective study to evaluate the association between the incidence of second cancers and initial treatments (chemotherapy, hormonal therapy, radiotherapy) which were used for breast cancer patients in Japan.

METHODS: Information of initial cancer treatments and second cancers on each patient was identified from the Osaka Cancer Registry. Coding of second cancers has followed the International Association Cancer Registry (IACR). We classified all patients according to each initial treatment (chemotherapy, hormonal therapy, radiotherapy, or no treatment). In each treatment group, the incidence rate for each type of second cancer was computed as the observed number of events divided by the total number of person-years at risk. The incidence rate ratio (IRR) associated with each treatment vs no treatment was estimated. In these calculations, patients were considered to be at risk from the date diagnosis of the primary breast cancer until the date of occurrence of each type of second cancer, the date of death, the last date which she was known to be alive, or the end of the study period (December 31, 2003), whichever occurred first. The effect of treatment adjusted for each covariate on second cancers was examined by using the stratified analysis. IRRs of hormonal therapy adjusted for covariates on all second cancers are evaluated by the Cox proportional hazards model. We considered covariates as the age at diagnosis, the stage of primary breast cancer, chemotherapy, radiotherapy and lymph node metastasis. With Yates' continuity correction, the chi-square values were calculated. All statistical analysis was performed using SAS9.1 or JMP 7.

RESULTS: The subjects of this study were 33,043 primary breast cancer patients who had been diagnosed during 1975-2003. The mean length of follow-up was 5.2 ± 4.3 years. 1,857 second cancers had occurred. The IRR associated with each treatment vs no treatment was evaluated according to site of second cancers (esophagus, stomach, colon, rectum, pancreas, lung, uterus cervix, corpus uterus, ovary, kidney, bladder, non-Hodgkin's lymphoma, thyroid, and acute myeloid leukemia (AML)). For hormonal therapy, the IRR of all second cancers was 0.64 (95% CI, 0.58 to 0.70), the IRR of corpus uterus cancer was 3.04 (95% CI, 1.78 to 5.19) For chemotherapy, the IRR of all second cancers was 0.91 (95% CI, 0.83 to 1.00). The risk of corpus uterus cancer was 2.32 (95% CI, 1.27 to 4.23) and the liver cancer was 0.54 (95% CI, 0.37 to 0.78). For radiotherapy, the IRR of all second cancers was 0.97 (95% CI, 0.87 to 1.08).The IRR of pancreas cancer was 0.37 (95% CI, 0.17 to 0.81). As for a result of

multivariate analysis, the IRR of all second cancers associated with hormonal therapy was 0.85 (95% CI, 0.77 to 0.95) after adjustment of covariates such as age at diagnosis, diagnosis year, various therapeutics, and lymph node metastasis. The IRR of corpus uterus cancer associated with hormonal therapy was 2.53 (95% CI, 1.41 to 4.55) after adjustment of covariates.

CONCLUSIONS: The incidence rate of all second cancers associated with initial cancer treatment was lower than that with the no treatment. Only the incidence of second corpus uterus cancer may be related to hormonal therapy.