FERTILITY OF FEMALES AFTER TREATMENT FOR CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

Daniel M. Green¹, Toana Kawashima², Wendy Leisenring², Marilyn Stovall³, Sarah Donaldson⁴, Charles A. Sklar⁵, Julianne Byrne⁶, Leslie L. Robison⁷

¹Department of Pediatrics, Roswell Park Cancer Institute, Buffalo, NY, USA
²Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
³Department of Radiation Physics, University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
⁴Department of Radiation Oncology, Stanford University Medical Center, Stanford, CA, USA
⁵Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA
⁶Department of Epidemiology & Biostatistics, George Washington University, Washington, DC
⁷Department of Epidemiology and Cancer Control, Saint Jude Children’s Research Hospital, Memphis, TN, USA

Abstract:

Background: Determine the proportion of female childhood cancer survivors with impaired fertility and evaluate impact of treatment on likelihood of pregnancy. Methods: 5665 CCSS participants and 1,735 siblings were classified as surgically sterile for contraceptive purpose vs. non-contraceptive purpose, impaired fecundity (ongoing attempts to become pregnant for a period of one year without success or use of medication to help achieve a pregnancy), or fecund. Cox proportional hazard modeling was used to estimate the relative risk of pregnancy (RR) for survivors versus siblings, controlling for education level, marital status, age at primary diagnosis, race/ethnicity, smoking status and fecundity group. Additional models among survivors, examine the impact of treatment variables on pregnancy. Results: Survivors were 6-30 yrs from cancer diagnosis (mean-16.3 yrs) and 15-44 yrs of age at the time of study (mean-25.1 yrs). 516 (9.1%) survivors or their partners were surgically sterile, 415 (7.3%) had impaired fecundity and 4734 (83.6%) were fecund. Among fecund subjects, the RR for pregnancy was 0.9 (p=0.0004) for survivors compared to siblings. The RR was 0.8 (p=0.12) among subjects with impaired fecundity. Multivariate analysis demonstrated that ovarian RT dose ≤ 250 cGy with a pituitary RT dose > 4000 cGy (RR=0.4; p=0.0005) or ovarian RT dose > 250 with a pituitary RT dose ≤ 4000 cGy (RR= 0.3  p=0.0001) or a pituitary RT dose > 4000 cGy (RR=0.2; p=0.01) and increasing AAS (1st tertile RR=0.9; p=0.4); 2nd tertile RR= 0.8; p=0.04; 3rd tertile RR=0.8; p=0.04) were independently associated with impaired fertility. In the multivariate analysis, neither a history of oophoropexy nor prior treatment with cis-platinum, cytosine arabinoside, doxorubicin or vinblastine remained statistically significant. Conclusions: Female survivors of childhood cancer have impaired fertility due in part to ovarian RT dose and increasing AAS.

Comment [g1]: