ASCO abstract

Non-Surgical Premature Menopause (NSPM) in the Childhood Cancer Survivor Study (CCSS): Prevalence, risk factors, and reproductive outcomes.

Background:

Female survivors of childhood cancers are at increased risk for NSPM, cessation of menses prior to age 40 not secondary to resection of reproductive organs. Our aims were to assess prevalence of and risk factors for NSPM and to examine the implications of NSPM on reproductive outcomes.

Methods:

Participants included 2930 female survivors diagnosed between 1970 and 1986 and enrolled in the original CCSS cohort (median age at diagnosis 6 years, range 0-20; median age at follow-up 34 years; range 18-59) who were older than age 18 at last follow-up without prior acute ovarian failure. They were compared to 1399 siblings (median age 38 years, range 19-63). Among survivors, multivariable logistic regression identified risk factors for NSPM. Pregnancy and live birth rates were compared between survivors with and without NSPM.

Results:

110 survivors developed NSPM [median age 32, range 16-40, prevalence of 9.1 % at age 40 (95% CI 4.9-17.2), relative risk 10.5 (95% CI 4.2-26.3) compared to siblings (0.9% at age 40, 95% CI 0.4-2.3)]. The prevalence was highest among survivors who received a cyclophosphamide equivalent dose (CED) > 6000 mg/m^2 (18.7% at age 40) or $\geq$ 5Gy RT to the ovaries (24.1%). Among survivors, independent risk factors included age > 14 at diagnosis (odds ratio [OR] 2.3, 95% Confidence Interval [CI] 1.4-3.8), CED ≥ 6,000 mg/m^2 (OR 3.6, 95% CI 2.1-6.3; referent group: CED=0), and any dose of RT to the ovaries (<5Gy, OR 4.0, 95% CI 1.9-8.5; $\geq$5Gy, OR 20.4, 95% CI 7.8-53.5). Survivors who developed NSPM were less likely to ever be pregnant (OR 0.41, 95% CI 0.22-0.68) or have a live birth (OR 0.35, 95% CI = 0.16-0.66; p = .0032) between the ages of 31-40 compared to those who did not. The same comparisons were not significant between the ages of 21-30.

Conclusion:

Ongoing follow-up of the original CCSS cohort enabled us to identify a threshold exposure to alkylating agents and older age at diagnosis as increasing the risk for NSPM among survivors. The development of NSPM is associated with lower rates of pregnancy and live birth after age 31. This information will assist clinicians counseling patients about their risk for early menopause and need for alternative reproductive options.