

Gastrointestinal Malignancies as a Second Malignant Neoplasm in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

Henderson, TO, MD, MPH¹, Whitton, J, MS², Leisenring, W, PhD², Neglia, J, MD³, Meadows, A, MD⁴, Crotty, C, MPH¹, Oeffinger, KC, MD⁵, Diller, L, MD⁶, Inskip, P, ScD⁷, Stovall, M, PhD⁸, Armstrong, G, MD⁹, Robison, LL, PhD⁹, Nathan, PC, MD, MSc¹⁰

¹University of Chicago, Chicago, IL, ²Fred Hutchinson Cancer Research Center, Seattle, WA, ³University of Minnesota, Minneapolis, MN, ⁴Children's Hospital of Philadelphia, Philadelphia, PA, ⁵Memorial Sloan-Kettering Cancer Center, New York, NY, ⁶Dana-Farber Cancer Institute/Children's Hospital Boston, Boston, MA, ⁷National Cancer Institute, Bethesda, MD, ⁸MD Anderson Cancer Center, Houston, TX ⁹St. Jude Children's Research Hospital, Memphis, TN, ¹⁰The Hospital for Sick Children, Toronto, Ontario

Background: There is emerging evidence that childhood cancer survivors (CCS) develop gastrointestinal (GI) malignancies more frequently and at an earlier age than the general population. We sought to determine the risk of GI second malignant neoplasms (SMN) and describe the factors associated with their development in order to inform surveillance recommendations.

Methods: We assessed the risk of GI SMN in a cohort of 14,372 5-year CCS and compared that to population data from the Surveillance, Epidemiology and End Results (SEER) program. Multivariate Cox regression models were fit to evaluate key factors' impact on GI SMN development.

Results: 45 CCS developed GI SMN at a median age of 33.5 years (range: 9.7-44.8) and a median of 22.8 years (range: 5.5-30.2) from their original diagnoses. The 30-year cumulative incidence of a GI SMN was 0.64% (95% confidence interval [CI]: 0.43-0.86). The most frequent SMN locations were colorectal (n=24; 53%), stomach (n=7; 16%), and hepatobiliary system (n=4, 9%). CCS with a GI SMN are more likely to be deceased than those without (51.1 vs. 13.8%, p<0.05) The risk of GI SMN was almost 5-fold higher in CCS than the general population (standardized incidence ratio=4.6, 95% CI: 3.5-6.1). Survivors of Wilms' tumor, Hodgkin's lymphoma and bone tumors were at highest risk. The multivariate model revealed that abdominal radiation (RR=5.32, 95% CI: 2.74-10.32), alkylating agents (RR=2.60, 95% CI: 1.06-6.37) and platinum drugs (RR=4.73, 95% CI: 1.49-15.14) increased the risk of GI SMN.

Conclusions: CCS are at increased risk for developing a GI SMN, and these neoplasms are associated with a significant risk of mortality. Surveillance in at-risk survivors should commence at a younger age than is recommended for the general population.