

**TITLE:** Late Cholecystectomy in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

**BACKGROUND:** Cholecystectomy (CCY) is among the most common operations performed in the developed world and is offered as a cure for symptomatic gallbladder disease. Whether survivors of childhood cancer undergo CCY at a higher rate than the general population is unknown.

**METHODS:** We identified 5-year survivors diagnosed between 1970 and 1999 who self-reported late (>5 years after cancer diagnosis) CCY. Rates of CCY were determined among the entire cohort and in association with various risk factors and treatment exposures. Adjusted rate ratios (ARR) were estimated with multivariable piecewise exponential models.

**RESULTS:** Among 24,248 survivors (median follow-up 22.3, interquartile range [IQR] 16.2-30.1 years) and 5,038 siblings (median follow-up 26.4, IQR 19.3-33.7 years), the unadjusted cumulative incidence of CCY at age 50 was 7.2% (n=757) in survivors and 6.5% (n=168) in siblings. After adjusting for age, sex and race/ethnicity, survivors underwent CCY at higher rates compared to siblings (ARR=1.3, 95% CI=1.1-1.5). Relative to siblings, acute lymphoblastic leukemia survivors underwent CCY at a higher rate (ARR=1.6, 95% CI=1.3-2.0), all other diagnoses were not independently associated with higher rates of CCY. Among survivors, risk factors for late CCY included female sex, increasing body mass index (BMI) class, exposure to platinum agents and total body irradiation (TBI) (Table).

**CONCLUSIONS:** CCY is performed more commonly among childhood cancer survivors relative to siblings. In addition to known risk factors for gallbladder disease, cancer treatment exposures may further enhance risk for CCY. Awareness and education regarding this observation may ensure timely diagnosis and treatment of symptomatic disease.

**TABLE.** Multivariable analysis of risk factors for late CCY among survivors.

	<b>ARR* (95% CI)</b>
Female sex	4.0 (3.2-5.1)
BMI (kg/m <sup>2</sup> ; ref 18.5-24.9)	
<18.5	0.7 (0.4-1.3)
25-29.9	1.8 (1.4-2.3)
30-39.9	2.7 (2.1-3.5)
≥ 40	4.1 (2.7-6.1)
Any platinum agent	1.5 (1.0-2.2)
TBI	3.2 (1.4-7.4)

\*also adjusted for attained age (as cubic splines), age at diagnosis, decade of diagnosis, race/ethnicity, insurance status, chemotherapy exposures, abdominal radiotherapy and stem cell transplant.