

Temporal trends among survivors of rhabdomyosarcoma: A report from the Childhood Cancer Survivor Study (CCSS)

Background: Intergroup Rhabdomyosarcoma Study Group (IRSG) protocols included treatment modifications, which may have ameliorated late health outcomes for rhabdomyosarcoma (RMS) survivors treated in more recent era.

Methods: We evaluated chronic health conditions (CHCs) and late mortality (>5 years from diagnosis) among survivors treated 1970-1990 (IRSG I-III) and 1991-1999 (IRSG IV), and associations with specific treatments to identify treatment-related factors for adverse outcomes. Associations between treatments and CHCs and mortality were evaluated using Fine and Gray's proportional hazards method accounting for competing risks.

Results: 856 survivors treated 1970-90 (median diagnosis age 5.4 years [0- 20]) and 306 treated 1991-99 (median diagnosis age 5.5 years [0-20]) were included. Significant exposure differences between eras included higher percentage (53% vs. 17%, $p < 0.01$) receiving $\geq 20\text{gm/m}^2$ cumulative alkylators in 1991-99, but more receiving platinum (13% vs 5%, $p < 0.01$) and abdomen/ pelvis radiation (29% vs. 23%, $p = 0.04$) in 1970-90. 20-year cumulative incidence for any (40% vs. 28%, $p < 0.01$), ≥ 2 (16% vs. 7%, $p < 0.01$), and endocrine (8% vs. 2.5%, $p < 0.01$) grade 3-5 CHCs was higher in 1970-90 compared to 1991-99. The hazard ratio (HR) for any (HR 0.7, 95% Confidence Interval [CI] 0.55-0.9), ≥ 2 (HR 0.38, 95% CI 0.22-0.66) and endocrine (HR 0.25, 95% CI 0.09-0.67) grade 3-5 CHC was lower for 1991-99 survivors than 1970-90. The effect of era (1991-99 vs 1970-90, HR 0.73; 95% CI 0.59-0.91) on CHC was not attenuated when treatment variables were added to multivariable model. Exposures with increased risk of grade 3-5 CHC included platinum (hearing, HR 2, 95% CI 1.07-3.8), anthracycline $\geq 250\text{mg/m}^2$ (cardiovascular, HR 2.7, 95% CI 1.2-6) and abdomen/ pelvis radiation (second malignant neoplasms, HR 2.1, 95% CI 1.1-4, gastrointestinal, HR 7.4, 95% CI 3.5-16 and endocrine, HR 2.5, 95% CI 1.4-4.4). Gonadal dysfunction was the most common endocrine CHC. There was no difference in all cause or cause-specific mortality between the two cohorts.

Conclusions: RMS survivors from the IRSG IV are at reduced risk for late onset chronic health conditions compared to previous era.

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