

Chronic health conditions (CHC) and late mortality in survivors of Acute Lymphoblastic Leukemia (ALL) in the Childhood Cancer Survivor Study.

Background: The impact of evolving risk-stratified therapy on long-term morbidity and mortality in survivors of childhood ALL remains largely unknown.

Methods: All-cause and health-related late mortality (HRM; captures death from late-effects occurring >5 yrs from diagnosis), subsequent (malignant) neoplasm [S(M)N], CTCAE graded CHC and neurocognitive outcomes were assessed in 5-yr survivors of ALL diagnosed <21 yrs of age from 1970-99. Therapy combinations defined 6 groups: 1970s-like (70s), standard and high risk 1980s- and 1990s-like (80sSR, 80sHR, 90sSR, 90sHR), relapse/transplant (R/BMT). Cumulative incidence and standardized mortality ratios (SMR) were calculated. Piecewise exponential and log-binomial models estimated rate ratios (RR) with 95% confidence intervals (CI).

Results: Among 6148 survivors (median age 31.5 yrs), 15-yr cumulative incidence of all-cause mortality was 5.8% (CI 5.3-6.2) and HRM was 1.5% (1.2-1.7). Compared to 70s, HRM was lower for 90sSR and 90sHR (RR 0.1, CI 0.0-0.3; 0.2, 0.1-0.7), similar to that in the US population (SMR; CI: 90sSR 1.1; 0.6-1.9, 90sHR 1.9; 0.8-3.7). 20-yr cumulative incidence of SN was 3.5% (CI 3.1-3.9). Compared to 70s, 90sSR had lower risk of benign meningioma (RR 0.1, CI 0.0-0.3) and SMN (0.3, 0.1-0.6) with no absolute excess risk compared to the US population. 90sSR was associated with a lower risk of CHCs (Table).

	Grade 3-5 CHC				Neurocognitive Impairment	
	Any	Congestive heart failure	Stroke	Major joint replacement	Task Efficiency	Memory
70s	1.0	1.0	1.0	1.0	1.0	1.0
80sHR	0.8 (0.7-1.1)	0.9 (0.3-2.6)	0.8 (0.3-1.8)	1.7 (0.4-7.6)	1.0 (0.7-1.3)	0.8 (0.6-1.1)
80sSR	0.9 (0.7-1.1)	0.6 (0.2-1.7)	1.6 (0.7-3.3)	2.3 (0.7-7.7)	1.0 (0.8-1.4)	0.8 (0.6-1.0)
90sHR	0.8 (0.6-1.1)	0.4 (0.1-1.6)	1.0 (0.3-3.0)	3.8 (1.5-9.3)	0.8 (0.6-1.2)	0.7 (0.5-0.96)
90sSR	0.4 (0.3-0.6)	0.0 (0.0-0.1)	0.4 (0.2-0.97)	1.9 (0.7-5.6)	0.5 (0.4-0.7)	0.6 (0.5-0.8)
R/BMT	2.3 (1.9-2.7)	1.9 (0.8-4.5)	4.0 (2.3-6.9)	5.6 (2.2-14.3)	0.9 (0.7-1.2)	0.8 (0.6-1.0)

RR(CI) adjusted for age at diagnosis, attained age, sex, race.

Conclusions: More recent risk-stratified therapy has succeeded in reducing risk of late mortality and CHCs among long-term survivors of ALL.

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