

Risk-adapted therapy for pediatric Hodgkin lymphoma (HL) results in lower risk of late effects: a report from the Childhood Cancer Survivor Study (CCSS)

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Background: The goal of multi-modal, risk-adapted therapy for HL is to increase cure rates while decreasing risk for late effects; this is particularly important for children due to their vulnerability to cytotoxic therapy and life expectancy.

Methods: Severe, disabling, life-threatening and fatal chronic conditions (CTCAE v4.03 grades 3-5) were determined for 2,996 5-yr HL survivors from CCSS diagnosed age <21 from 1970-1999. Cox models evaluated hazard ratios (HR) and 95% confidence intervals (CI), comparing risks of grade 3-5 chronic conditions by age 40 among treatment regimens with historical total lymphoid irradiation (TLI) as the referent group.

Results: HL survivors were a mean age of 35.6 years (range, 12-58). The cumulative incidence of any grade 3-5 condition by age 40 was 43.6% (95% CI 41.1-46.1). Risk-adapted therapy using 'hybrid' chemotherapy with or without radiotherapy (RT) was associated with a substantial reduction in risk for serious late effects (Table). While omitting radiation was associated with a 3-fold reduction in risk of late effects, HL survivors with a history of recurrence and/or a hematopoietic transplant (HCT) had an overall risk similar to those treated with TLI.

Table. HR (95% CI) for selected treatment groups, adjusted for sex, age at HL, and other treatment regimens, for a grade 3-5 condition, subsequent malignant neoplasm (SMN), cardiopulmonary disease (CPD), or endocrinopathy (Endo)

Treatment Group	N	CTCAE Grade 3-5 Chronic Condition			
		Any	SMN	CPD	Endo
TLI \geq 35 Gy (referent)	570	1.0	1.0	1.0	1.0
Recurrence or HCT	296	1.2 (0.9-1.5)	0.6 (0.4-0.9)	2.2 (1.6-3.1)	0.9 (0.6-1.4)
Chest RT ⁰ 15.0 - 34.9 Gy + hybrid* chemo	383	0.7 (0.5-0.9)	0.7 (0.5-1.1)	0.7 (0.4-1.1)	0.8 (0.6-1.2)
Hybrid chemo without RT	216	0.3 (0.2-0.4)	0.4 (0.2-0.8)	0.3 (0.1-0.8)	0.2 (0.1-0.5)

⁰with / without abdominal RT; *hybrid chemotherapy including an anthracycline plus an alkylator

Conclusions: Risk-adapted therapy has resulted in a reduction in serious long-term outcomes. While omitting radiotherapy is associated with a further reduction in risk, this consideration must be balanced with the risk of recurrence and the serious morbidity associated with salvage therapy.