Sex-Specific Vascular Sequelae of Mediastinal Radiotherapy in Adolescent-and-Young-Adult Hodgkin Lymphoma: A 44-Year SEER Analysis Using Competing-Risk and Life-Years-Lost Modelling

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BACKGROUND

Adolescent and young adult (AYA; 15–39 years) survivors of Hodgkin lymphoma (HL) are at elevated risk for late cardiovascular mortality, particularly following mediastinal radiotherapy (RT). However, population-level estimates of this risk, stratified by treatment era, sex, and socioeconomic status (SES), remain poorly defined.

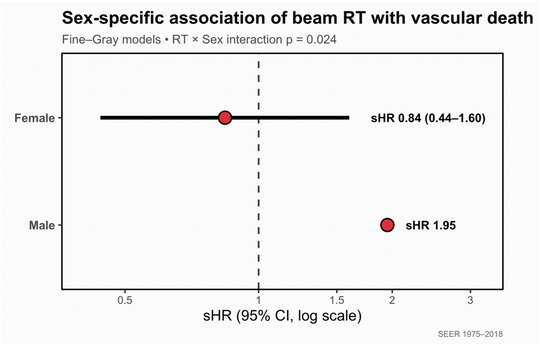
OBJECTIVE

To assess RT utilization trends, quantify long-term vascular mortality, examine sex-specific effects, and estimate restricted life-years lost (YLL) among AYA HL survivors using SEER-8 data (1975–2018)

Methodology

We identified 4,420 first-primary AYA HL cases with complete survival data (median follow-up: 151 months). Beam-RT, chemotherapy, stage, sex, and county-level SES were abstracted. The primary outcome was death from cardiovascular or cerebrovascular causes; non-vascular deaths were treated as competing events. Cumulative incidence functions (CIFs) and Fine–Gray regression were used to estimate sub distribution hazard ratios (sHRs), including interaction terms (RT × sex, age, SES). A 5-year landmark analysis evaluated risk durability, and 30-year restricted YLL was derived by integrating CIFs.

Sex-Specific Association of beam RT with vascular death



KEYWORDS

Hodgkin Lymphoma, Mediastinal Radiotherapy, Cardiovascular Mortality, SEER Registry

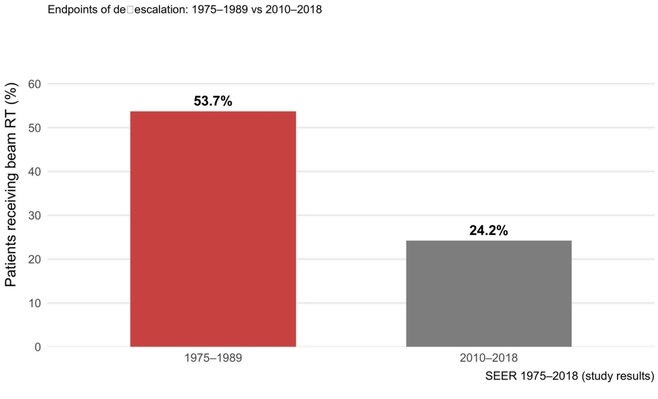
FINANCIAL DISCLOSURE

This author declares no competing financial interests.

RESULTS

RT use declined from 53.7% (1975–1989) to 24.2% (2010–2018) (OR = 0.46; p = 0.001). The 20-year vascular death CIF was 4.0% with RT vs 3.0% without (p = 0.007). Among patients who survived at least five years, the cumulative incidence of vascular death remained elevated with prior RT: 8.0% versus 4.8% in those not exposed (p = 0.009). RT was independently associated with elevated vascular mortality (sHR = 1.53; 95% CI 1.10–2.11; p = 0.011), persisting in the landmark model (sHR = 1.55; p = 0.011). A significant RT × sex interaction localized excess risk to males (effective sHR ≈ 1.95); no effect was seen in females (sHR ≈ 0.84; p interaction = 0.024). RT × age and RT × SES interactions were nonsignificant. RT was associated with an average excess of 0.15 life-years (≈55 days) lost per patient. RT de-escalation occurred equitably across SES strata (all interaction p > 0.3).

Beam Radiotherapy use in AYA Hodgkin Lymphoma



CONCLUSION

Despite declining use, mediastinal RT continues to confer a ~50% increase in vascular mortality, almost exclusively in males. Sex-specific survivorship care and RT-sparing strategies remain essential for long-term cardiovascular health in AYA HL survivors.

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