LONG-TERM OUTCOMES IN HODGKIN LYMPHOMA SURVIVORS: A REAL-WORLD MATCHED COHORT COMPARISON OF RADIATION PLUS CHEMOTHERAPY VERSUS CHEMOTHERAPY ALONE

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Introduction

- Hodgkin lymphoma (HL) is a highly curable malignancy, and combined modality therapy with chemotherapy and radiation has historically improved disease control.
- However, long-term survivorship concerns have emerged, particularly regarding late toxicities associated with radiation, including cardiovascular disease, infections, and secondary malignancies.
- Despite advances in treatment, real-world comparative data on long-term outcomes in patients treated with radiation plus chemotherapy (RT+CT) versus chemotherapy alone (CT) remain limited. Understanding these risks is critical to guide treatment decisions and survivorship care planning.

Aim

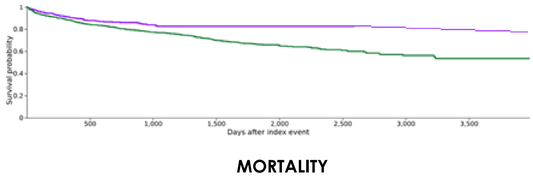
- This study aimed to evaluate and compare the long-term outcomes of Hodgkin lymphoma survivors treated with RT+CT versus CT alone in a large, real-world cohort.

Objectives

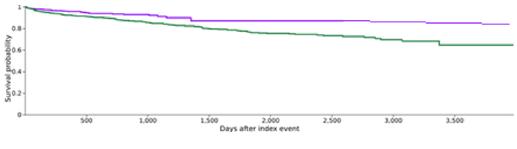
- To assess differences in long-term all-cause mortality between patients treated with RT+CT and CT alone.
- To evaluate the incidence of major late complications, including infections, transfusion requirements, cardiovascular events, organ dysfunction, and secondary malignancies.
- To provide real-world evidence to inform treatment strategies that balance disease control with survivorship quality.

Methods

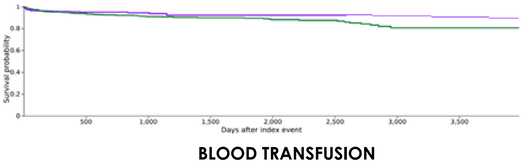
- We conducted a retrospective cohort study using the TriNetX global network. Adult patients (age 18–99) diagnosed with Hodgkin lymphoma between 2013–2023 were identified.
- Two cohorts were defined: those receiving RT+CT and those receiving CT alone. Propensity score matching (1:1) was performed across baseline demographics and clinical variables, resulting in two balanced cohorts (n=12,413 per group)
- Outcomes were followed for up to 10 years, starting one day after the first qualifying therapy. The primary endpoint was long-term all-cause mortality.
- Secondary endpoints included cardiac arrest, infections, cytopenias, transfusion requirements, acute organ dysfunction, venous thromboembolism, and secondary hematologic or solid malignancies.
- Hazard ratios, risk differences, and 95% confidence intervals were calculated.



MORTALITY



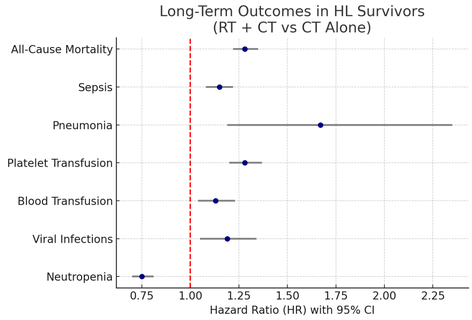
SEPSIS



BLOOD TRANSFUSION

Results

- Long-term all-cause mortality was significantly higher in the RT+CT group (28.7%) compared to the CT alone group (21.5%), corresponding to a 7.3% absolute risk increase and a hazard ratio of 1.28 (95% CI 1.22–1.35, p<0.001).
- RT+CT was associated with higher rates of sepsis (15.6% vs 13.5%, p<0.001), pneumonia (1.0% vs 0.6%, p=0.003), platelet transfusion (13.4% vs 10.5%, p<0.001), blood transfusion (9.9% vs 8.8%, p=0.003), and viral infections (3.8% vs 3.2%, p=0.008).
- Neutropenia was less frequent with RT+CT (15.1% vs 20.1%, p<0.001).
- There were no significant differences between the groups in the incidence of cardiac arrest, myocardial infarction, heart failure, venous thromboembolism, acute kidney injury, gastrointestinal toxicities, pericardial disease, pulmonary fibrosis, or respiratory support requirements. Rates of most secondary hematologic and solid malignancies, including breast, lung, thyroid, and colorectal cancers, were also similar across cohorts (all p>0.05).



Summary

- In this large real-world cohort study of over 24,000 matched Hodgkin lymphoma survivors, treatment with radiation plus chemotherapy (RT+CT) was associated with significantly higher long-term mortality compared to chemotherapy (CT) alone.
- RT+CT was also linked to increased risks of sepsis, pneumonia, viral infections, and transfusion requirements, while neutropenia was less frequent in this group.
- Importantly, there were no statistically significant differences in the incidence of major cardiovascular events, venous thromboembolism, acute organ dysfunction, or secondary hematologic and solid malignancies.

Discussion

- These findings highlight a complex tradeoff in the long-term management of HL survivors. Although radiation historically contributed to improved disease control, its addition to chemotherapy appears to increase the burden of late toxicities that negatively impact overall survival.
- The excess mortality observed was not explained by classic concerns such as secondary cancers or cardiovascular disease, but rather by infections and transfusion dependence, suggesting long-term immune and marrow suppression as key drivers.
- It should also be noted that radiation is sometimes used in patients with bulky or more advanced disease which may introduce residual confounding and partially account for differences in outcomes despite propensity matching.
- In the context of modern treatment advances, including effective chemotherapy regimens, targeted agents, and immunotherapies, the necessity of routine radiation should be re-examined.
- Tailored approaches that minimize exposure to RT without compromising initial disease control may improve survivorship outcomes. Ongoing vigilance in survivorship care, with focus on infection prevention, supportive care, and careful long-term monitoring, will be essential for optimizing quality and duration of life in HL survivors.

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