Reduction in Cardiac Radiation Dose Among Children Receiving Mediastinal RT: Comparison of Involved-Site vs Involved-Field RT Delivered in Three Children's Oncology Group Trials.

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Introduction

Delayed cardiac toxicity is a potential complication of treatment among survivors of pediatric Hodgkin Lymphoma (HL) treated with mediastinal radiation therapy (RT). The transition from involved-field RT (IFRT) to more conformal involved-site RT (ISRT) was intended to reduce normal tissue exposure among patients treated on Children's Oncology Group (COG) trials. We evaluated the cardiac dose received by patients treated on three COG trials to determine whether ISRT had achieved this goal.

Methods

Cardiac radiation dose was determined for patients with available RT-DICOM data submitted to IROC for patients treated with mediastinal RT on COG trials AHOD 0031[1] (treated with IFRT to all involved sites, N=87 with evaluable DICOM RT plans), AHOD 0831[2] (IFRT to sites of bulk or slow response; N=121) and AHOD 1331 (treated with ISRT to large mediastinal adenopathy (LMA) or slow early response; N=227). For each patient we calculated the mean heart dose and percent volume of heart receiving ≥20Gy (V20), both of which have been shown previously to be correlated with delayed cardiotoxicity, and compared heart doses between AHOD 1331 (ISRT) and AHOD 0831 and AHOD 0031 (IFRT).

Results

There was a significant decline in the percentage of patients who received protocol directed RT in more recent studies: 93.8%, 75.8% and 45.8% respectively in AHOD 0031 (standard arm), AHOD 0831 and AHOD 1331. The heart doses among patients getting mediastinal ISRT on AHOD 1331 were significantly lower (median of mean heart doses = 10.1Gy) compared to IFRT used on AHOD 0831 (13.8Gy) and AHOD 0031 (14.5Gy), $p<0.05$. Similarly, the cardiac V20 was also significantly lower with ISRT on AHOD 1331. Patients receiving mediastinal ISRT on AHOD 1331 for LMA had a lower mean heart doses (median value =

10.1Gy) than those with LMA on the older studies (15.2Gy on AHOD 0031 and 14.1Gy on AHOD 0831).

Conclusion

The transition to ISRT on COG AHOD 1331 was associated with a significant decrease in cardiac heart dose compared to prior trials that used IFRT. Based on dose-risk data from the Childhood Cancer Survivor Study[3], these results suggest that compared to chemotherapy alone, mediastinal ISRT as used on AHOD 1331 could increase the 30-year cumulative incidence of heart disease by approximately 0.5-2% for all patients on the trial and 1-4% for those getting mediastinal RT.

Affix

References

[1] Friedman, D. L., L. Chen, et al. (2014). "Dose-Intensive Response-Based Chemotherapy and Radiation Therapy for Children and Adolescents With Newly Diagnosed Intermediate-Risk Hodgkin Lymphoma: A Report From the Children's Oncology Group Study AHOD0031." Journal of Clinical Oncology 32(32): 3651-3658.

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[3] Bates, J. E., M. R. Howell, et al. (2019). "Therapy-related cardiac risk in childhood cancer survivors: An analysis of the childhood cancer survivor study". Journal of Clinical Oncology, *37*(13): 1090-1101