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Late Effects of Mediastinal Radiotherapy in Pediatric and Young Adult Hodgkin's Lymphoma Survivors: A Retrospective Records Review

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Introduction

Hodgkin's Lymphoma (HL) has become highly curable; in the pediatric and young adult setting, five-year survival exceeds 95%.[1] Therefore, understanding and minimizing the long-term negative effects of treatment is essential in successful care. Mediastinal radiotherapy (MRT) is a central component of treatment, used when first-line chemotherapy does not eradicate disease. In the heart, radiation most commonly causes pericarditis, but can commonly also lead to coronary artery disease and valve disease.[2] Late Effects Clinics in major hospitals can screen for these effects and more, but practices vary widely.[3] Radiotherapeutic doses have decreased by nearly 70 percent in HL patients over the last three to four decades, and there is a need for up-to-date information about the true risks faced by new patients.[4]

Methods

Medical records were reviewed for patients meeting these criteria:

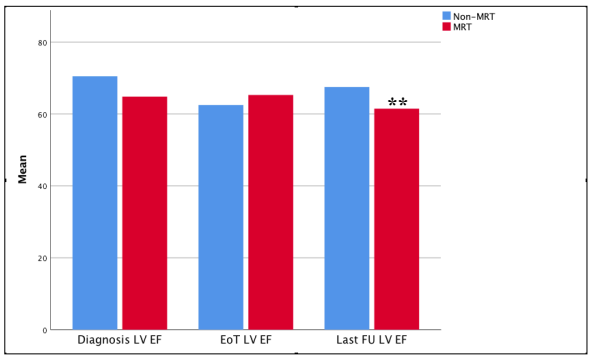
- Diagnosed with HL under 40 years of age
- Diagnosed with HL between 2002 and 2013
- At least one follow-up appointment 12 months after treatment

Demographic and treatment data were collected, including:

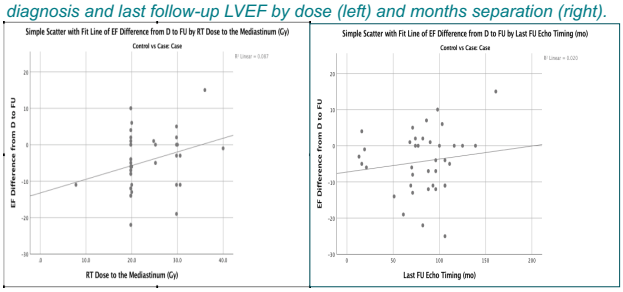
- Current age, and age at diagnosis; diagnosis histology and stage
- Cardiovascular risk factors including diabetes, BMI, smoking, and family history
- Chemotherapy and radiotherapy regimens: dose, field, and fractions

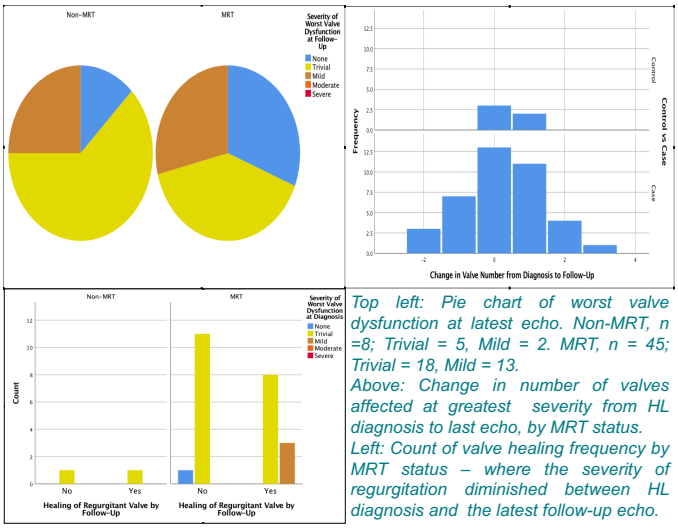
Cardiac functional measurements relied on echocardiograms taken before, at the end of, and long after treatment, examining:

- Systolic function (by ejection fraction) and diastolic function
- Valvular stenosis and regurgitation
- Pericardial Effusion



*Above: Bar graph of left ventricular ejection fraction (LVEF) at diagnosis, end-of-treatment, and latest follow-up. Left to right, n = 11, 67, 4, 23, 8, 44. ** p = 0.005 compared to diagnosis. Below: scatter plots of the difference between diagnosis and last follow-up LVEF by dose (left) and months separation (right).*

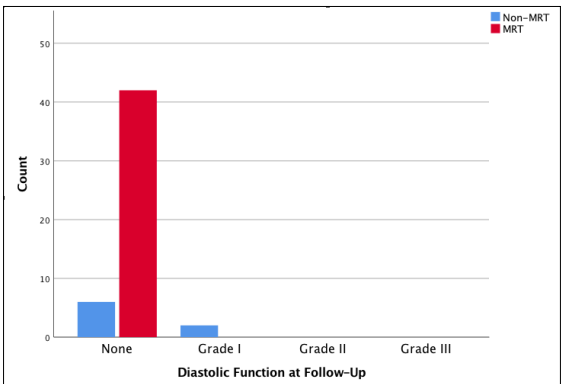




Top left: Pie chart of worst valve dysfunction at latest echo. Non-MRT, n =8; Trivial = 5, Mild = 2. MRT, n = 45; Trivial = 18, Mild = 13.
Above: Change in number of valves affected at greatest severity from HL diagnosis to last echo, by MRT status.
Left: Count of valve healing frequency by MRT status – where the severity of regurgitation diminished between HL diagnosis and the latest follow-up echo.

Results

Our cohort was comprised of 91 MRT patients and 27 non-MRT patients. Median follow-up for the entire cohort was 82 months. Mean anthracycline dose was 158 mg/m2. Within the MRT group, mean left ventricular ejection fraction (LVEF) decreased from 65.9% to 61.1% (left, p = 0.001). No significant change was seen within the non-MRT group. This decrease was present despite no linear association with either radiation dose to the mediastinum or length of time between first and last echocardiograms. There was no significant increase in severity or prevalence of cardiac valve dysfunction during the study period (above, p = 0.356 and 0.755 respectively).The non-MRT patients more commonly developed diastolic dysfunction by their most recent echocardiogram (below, p = 0.001). The non-MRT patients also more often demonstrated hypertension (NICE grade I) during follow-up (not shown, p = 0.005). Pericardial effusion did not differ significantly by MRT status.



Clustered bar graph of patients with diastolic dysfunction according to British Society of Echocardiography grading, split by MRT status.[5] p = 0.001.

Conclusions

This study suggests MRT may negatively impact on LVEF early in follow-up. Further research is required to investigate whether this is progressive, and the strength of its dose-dependent relationship among modern radiotherapy regimens. This study was limited by a small sample size and an inability to complete data collection. Still, demonstrating negative relationships between MRT and hypertension or diastolic dysfunction, our data suggest that these associations are not straightforward. Further research with larger sample sizes and longer follow-up is necessary to elucidate this effect. Should MRT again be shown to be protective, there would be a need for research examining the biological pathways producing this effect. These results will also enhance late effects care at UCLH and inform a detailed, prospective study of CV morbidity in patients treated with MRT.

References

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