Modern radiotherapy for Hodgkin lymphoma - associated radiation doses and predicted second cancer risks

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Introduction

Radiotherapy (RT) treatment for Hodgkin lymphoma (HL) has evolved: it is now often reserved for patients with slow or incomplete response to induction chemotherapy; prescribed doses are reduced; extended-field treatments have been replaced by involved field/site/node treatments; intensity modulated RT is used instead of conventional 2- or 3-dimensional conformal RT, improving dose conformity. Consequently, exposure to organs near the tumor site has been substantially reduced. However, risk estimates for radiation-related second cancers are based on patients treated decades ago due to the long follow-up needed to observe them. To better accommodate current doses in risk predictions we use details on the dose distribution to the organ of interest, and illustrate our method by predicting second breast cancer (BC) risk.

Methods

We estimated relative risks and age-specific incidence for BC and competing events (mortality or other subsequent cancer) from 1194 female Dutch 5-year HL survivors, treated at ages 11-40 during 1965-2000. To capture the radiation dose distribution in the breast, predictors were doses to 10 breast segments, and other BC risk factors. Models were validated in the North American Childhood Cancer Survivor Study cohort.

We then compared radiation dose distributions to the breast given in 2006-2021 among 101 patients with HL or other lymphoma in 1 German and 2 Dutch hospitals with doses received by 505 Dutch HL patients treated 1965-1997. Absolute BC risks 25 years after historic and recent treatments were estimated for low- and high-risk profiles.

Results

The average mean breast dose decreased from 21.4 Gy for historic to 3.0 Gy for recent treatments. The percentage of breast volume receiving >=20 Gy decreased from 48.7 to 2.2%. The minimum dose received by 20% of the breast volume decreased from 39.0 to 2.8 Gy. Using quadrant-specific doses, median absolute BC risk 25 years after HL treatment decreased from 21.0 to 6.9% for historic versus recent treatments for a high-risk patient and from 3.1 to 0.9% for a low-risk patient, respectively. Using mean dose instead of quadrant-specific doses, median absolute BC risks decreased from 20.3 to 6.0% and from 3.1 to 0.9% for the high- and low-risk patients, respectively.

Conclusion

Incorporating detailed organ-specific dose information in predictions of second BC risk can accommodate temporal changes in dose distributions. For breast cancer, substantially reduced contemporary RT doses lead to considerably lower risk estimates.

References

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