# Radiation-Induced CAD: Gender Disparities for Patients with Hodgkin's Lymphoma Following Radiation

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## INTRODUCTION

- Radiation-induced coronary artery disease (CAD) has become a more increasingly recognized phenomenon.
- Although the clinical relationship between radiation therapy and CAD risk is well known, there has been very little investigation of the gender relationship to radiation-induced CAD as well as how gender may contribute to increased cardiovascular (CV) mortality.
- Data comparison between Hodgkin's Lymphoma following treatment with radiation and the subsequent incidence of CAD has shown inconsistent results in terms of the role gender has on mortality.
- Our clinical hypothesis was that patients with Hodgkin's Lymphoma treated with radiation will have higher incidence of CV mortality in female patients due to the increased the risk of severe atherosclerotic lesions.

## METHODOLOGY

- We performed an aggregate data meta-analyses on 10 studies consisting of **13,975 patients with both coronary artery disease and Hodgkin's Lymphoma following radiotherapy.**
- We analyzed both all-cause mortality and cardiovascular clinical outcomes:

→ **nonfatal myocardial infarction (MI)**

→ **repeat revascularization**

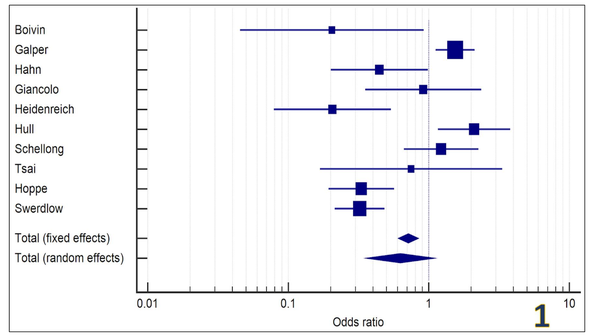
→ **stroke and a composite end-point of all of the above mentioned outcomes i.e. major adverse cardiac and cerebrovascular events (MACCE)] to examine the disparities between genders.**

- We also performed a meta-regression analysis to evaluate the effect of age on mortality for men versus women with both Hodgkin's lymphoma treated with radiation and CAD.
- Summary odds ratios (OR) and 95% confidence intervals (CI) were estimated using random-effects model.
- This systematic review and meta-analysis was conducted by the principles set in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA Statement.
- Q statistic of Chi-square value test and I2 index (inconsistency index) were used to evaluate the heterogeneity of individual studies contributing to the pooled estimate.
- An electronic database search was performed through MEDLINE/PUBMED, EBSCO, EMBASE, Thomson Reuters' Web of Science, the Cochrane Library, Google Scholar, and Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov
- We utilized standardized methods searching for the following keywords: "Radiation-Induced Coronary Artery Disease, Hodgkin's Lymphoma, Radiation, Mediastinal Tumors."
- As recommended by the Grading of Recommendations Assessment, Development and Evaluation Working Group methodology, two reviewers independently assessed all the critical outcomes in the following domains:

→ **of bias, inconsistency, indirectness, imprecision and publication bias.**

- Quality assessment was performed by two different assessors and a third assessor in case of discrepancies.

## FIGURES




| Study | Intervention | Controls | Odds ratio | 95% CI | z | P | Weight (%) Fixed | Weight (%) Random |
|---|---|---|---|---|---|---|---|---|
| Boivin | 2/300 | 12/378 | 0.205 | 0.0455 to 0.922 | | | 1.50 | 6.76 |
| Galper | 117/685 | 70/594 | 1.542 | 1.121 to 2.122 | | | 33.31 | 12.15 |
| Hahn | 12/49 | 32/76 | 0.446 | 0.201 to 0.987 | | | 5.37 | 10.16 |
| Giancolo | 14/32 | 17/37 | 0.915 | 0.353 to 2.370 | | | 3.74 | 9.37 |
| Heidenreich | 5/441 | 28/531 | 0.206 | 0.0789 to 0.538 | | | 3.68 | 9.33 |
| Hull | 145/162 | 203/253 | 2.101 | 1.164 to 3.790 | | | 9.74 | 11.14 |
| Schellong | 20/472 | 23/660 | 1.225 | 0.665 to 2.258 | | | 9.08 | 11.04 |
| Tsai | 15/31 | 5/9 | 0.750 | 0.169 to 3.333 | | | 1.52 | 6.81 |
| Hoppe | 17/916 | 71/1316 | 0.332 | 0.194 to 0.567 | | | 11.80 | 11.37 |
| Swerdlow | 28/2680 | 138/4353 | 0.322 | 0.214 to 0.486 | | | 20.26 | 11.86 |
| Total (fixed effects) | 375/5768 | 599/8207 | 0.714 | 0.603 to 0.846 | -3.901 | <0.001 | 100.00 | 100.00 |
| Total (random effects) | 375/5768 | 599/8207 | 0.627 | 0.353 to 1.113 | -1.594 | 0.111 | 100.00 | 100.00 |

**Test for heterogeneity**

| | |
|---|---|
| Q | 71.2734 |
| DF | 9 |
| Significance level | P < 0.0001 |
| $I^2$ (inconsistency) | 87.37% |
| 95% CI for $I^2$ | 78.78 to 92.48 |

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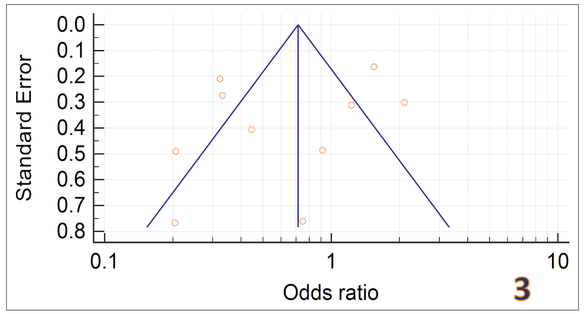
- Figure 1: Meta-Analysis of Binary Outcome Measures- Forest Plot
- Figure 2: Data compiled for Forest Plot




- Figure 3: Funnel plot analysis did not reveal asymmetry around the axis for the treatment effect in the following outcomes ($p < 0.05$ by Begg and Mazumdar's test or Egger's test).

## RESULTS

- In 13975 patients including 41% females and 59% males, **cardiovascular mortality was much higher in women compared to men (OR 0.64, 95% CI 0.64-0.93, p <0.006).**
- All-cause mortality was also higher in women compared to men (OR 0.70, 95% CI 0.45-0.96, p <0.001).
- On meta-regression, when plotting log odds ratio of cardiovascular mortality among males versus females (y-axis) against age (x-axis), **females had higher mortality with advancing age as well (coefficient = 0.111, p=0.001).**

## CONCLUSION

- For patients with both Hodgkin's lymphoma treated with radiation and CAD, women had a markedly higher rate of cardiovascular mortality compared to men.
- All-cause mortality was also significantly lower in men compared to women.
- Meta-regression showed a trend towards increased mortality among women with advancing age that reached statistical significance.
- Not only is survival impacted, but radiation-induced coronary artery disease among patients with Hodgkin Lymphoma has a significant impact on readmissions and hospital costs every year.
- Going forward, there needs to be increased surveillance and follow-up for female patients that have had Hodgkin's Lymphoma for the development of CAD to prevent higher cardiovascular mortality.

## REFERENCES

- Available Upon Request

## DISCLOSURES: NONE