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# Risk of Secondary Malignancies in Ovarian Cancer Survivors: 54,305 Patients Analyzed With 40 Years of Follow-up

A C. Casper

M W. Parsons

J Chipman

L M. Burt Jr

G Suneja

*See next page for additional authors*

## Authors

A C. Casper, M W. Parsons, J Chipman, L M. Burt Jr, G Suneja, K A. Maurer, and D K. Gaffney

# Risk of Secondary Malignancies in Ovarian Cancer Survivors: 54,305 Patients Analyzed With 40 Years of Follow-up

A. C. Casper[1], M. W. Parsons[2], J. Chipman[2], L. M. Burt Jr[3], G. Suneja[3], K. A. Maurer[4], and D. K. Gaffney[2]; [1]*Spokane Teaching Health Center, Spokane, WA,* [2]*University of Utah Huntsman Cancer Institute, Salt Lake City, UT,* [3]*Department of Radiation Oncology, Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT,* [4]*University of Utah, Salt Lake City, UT*

## BACKGROUND/AIM

- Survivors of ovarian cancer are at risk of developing secondary malignancy at various sites[1].
- As chemotherapy and radiation therapy are known to cause secondary malignancy, we sought to evaluate this risk in individuals who have had ovarian cancer[2].
- Understanding the sites where secondary malignancies develop and associated risk factors can help establish and inform screening protocols and assist the providers working with these patients.

## METHODS

- Standardized incidence ratios (SIR, observed-to-expected [O/E] ratio) and absolute excess risk (AER) of secondary malignancy were assessed in 54,305 patients diagnosed with ovarian cancer as a first malignancy between 1975 and 2016 in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program[3].
- The SIRs take into account age at diagnosis, year of diagnosis, and patient-years at risk.
- Risk of secondary malignancy was then stratified according to type of treatment, age, race, and latency from diagnosis.

## RESULTS

| | Patients 54,305 | | Patient Years 350,891 | | |
|---|---|---|---|---|---|
| Site | Observed | Excess Risk | O/E | 95% CI | |
| All sites | 3,981 | 12.7 | **1.13*** | 1.09 | 1.16 |
| All Solid Tumors | 3,450 | 9.48 | **1.11*** | 1.07 | 1.14 |
| Colon Excluding Rectum | 446 | 2.57 | **1.25*** | 1.14 | 1.38 |
| Rectum | 162 | 1.5 | **1.48*** | 1.26 | 1.73 |
| Pancreas | 153 | 0.93 | **1.27*** | 1.08 | 1.49 |
| Soft Tissue | 29 | 0.29 | **1.55*** | 1.04 | 2.22 |
| Vagina | 21 | 0.4 | **2.99*** | 1.85 | 4.57 |
| Bladder | 145 | 1.06 | **1.34*** | 1.13 | 1.58 |
| Kidney and Renal Pelvis | 109 | 0.61 | **1.25*** | 1.02 | 1.5 |
| Thyroid | 109 | 1.06 | **1.52*** | 1.25 | 1.83 |
| Leukemia | 235 | 3.88 | **2.38*** | 2.09 | 2.7 |

Table 1: SIR and AER for sites of secondary malignancy in ovarian cancer survivors that are significantly different when compared to a matched population.

| Race | O/E | 95% CI | |
|---|---|---|---|
| White | **1.09*** | 1.06 | 1.16 |
| Black | **1.43*** | 1.25 | 1.63 |
| Other | **1.55*** | 1.37 | 1.75 |

Table 2: SIR of secondary malignancy in ovarian cancer survivors according to race.

| | Chemotherapy | | | | | No Chemotherapy | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Patients 36,877 | | Patient Years 192,541 | | | Patients 17,428 | | Patient Years 158,349 | | |
| Site | Observed | Excess Risk | O/E | 95% CI | | Observed | Excess Risk | O/E | 95% CI | |
| All sites | 2,173 | 11.35 | **1.11*** | 1.07 | 1.16 | 1,808 | 14.35 | **1.14*** | 1.09 | 1.2 |
| All Solid Tumors | 1,869 | 7.34 | **1.08*** | 1.03 | 1.13 | 1,581 | 12.08 | **1.14*** | 1.08 | 1.2 |
| Leukemia# | 164 | 5.73 | **3.06*** | 2.61 | 3.56 | 71 | 1.64 | **1.57*** | 1.23 | 1.99 |

Table 3: SIR and AER for ovarian cancer survivors compared by receipt of chemotherapy

| | EBRT | | | | | No RT | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Patients 2,045 | | Patient Years 17,252 | | | Patients 52,260 | | Patient Years 33,638 | | |
| Site | Observed | Excess Risk | O/E | 95% CI | | Observed | Excess Risk | O/E | 95% CI | |
| All sites# | 244 | 41.61 | **1.42*** | 1.24 | 1.61 | 3,737 | 11.21 | **1.11*** | 1.08 | 1.15 |
| All Solid Tumors# | 203 | 29.68 | **1.34*** | 1.16 | 1.53 | 3,247 | 8.44 | **1.09*** | 1.06 | 1.13 |
| Bladder# | 15 | 5.6 | **2.81*** | 1.57 | 4.63 | 130 | 0.82 | **1.27*** | 1.06 | 1.51 |

Table 4: SIR and AER for ovarian cancer survivors compared by receipt of radiotherapy

| Site | Age (years) | Observed | AER | O/E | 95% CI | |
|---|---|---|---|---|---|---|
| All sites | 0-24 | 25 | 9.48 | 1.51 | 0.97 | 2.22 |
| | 25-49 | 1,025 | 24.69 | **1.43*** | 1.34 | 1.52 |
| | 50-74 | 2,539 | 11.1 | **1.09*** | 1.05 | 1.13 |
| | 75+ | 383 | -31.34 | **0.82*** | 0.74 | 0.91 |

Table 5: SIR for secondary malignancy according to age of primary diagnosis of ovarian cancer

1. Survivors of ovarian cancer are at increased risk of developing a secondary malignancy compared to a matched population (O/E 1.13). (Table 1)
2. Non-White patients were shown to be at higher risk of developing secondary malignancy when compared to White patients. (Table 2)
3. Chemotherapy was associated with an increased risk of leukemia but was not associated with an increased risk of overall or solid tumor secondary malignancy. (Table 3)
4. Radiotherapy was associated with an increased risk of overall and solid tumor secondary malignancy, but the only specific site which had an increased risk was the bladder. (Table 4)
5. Risk of secondary malignancy was increased in younger age groups, with patients between the ages of 25-49 having the highest risk of developing a secondary malignancy. (Table 5)
6. Risk of developing a solid tumor secondary malignancy was highest at latencies of 10-20 years. (Data not shown)

* Indicates a significant difference compared to the endemic rate
\# Indicates a significant difference between the two treatment groups

## CONCLUSIONS

- This is the largest study to examine the risk of secondary malignancy in patients with ovarian cancer and has the longest follow-up.
- The risk of secondary malignancy was elevated among survivors of ovarian cancer and varied with treatment modality, age, race, and latency.
- Chemotherapy and radiation were associated with an increased risk of secondary malignancy at specific sites, but chemotherapy was not associated with an increased risk of overall secondary malignancy.

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## CONTACT INFORMATION

Anthony.Casper@providence.org
Matthew.Parsons@hci.utah.edu
David.Gaffney@hci.utah.edu