Average Age of Diagnosis of Ovarian Cancer for Women with Pathogenic Variants in *BRIP1, RAD51C* and *RAD51D*

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BACKGROUND

- Recently, it has been shown that pathogenic variants (PVs) in *BRIP1*, *RAD51C* and *RAD51D* confer an increased lifetime risk of ovarian cancer (5.8–14.8%).
- As such, the NCCN now recommends that risk-reducing salpingo-oophorectomy (RRSO) be considered for women with PVs in these genes, in addition to several high-penetrance genes.[1]
- Based on the average age at diagnosis, RRSO is recommended between the ages of 35 and 40 for women with PVs in *BRCA1* and as late as 45 for women with PVs in *BRCA2.*
  - There are no specific age recommendations for women with PVs in *BRIP1*, *RAD51C*, or *RAD51D*.
- Here, we investigated the average age at diagnosis for women with ovarian cancer who carry a PV in *BRIP1*, *RAD51C*, or *RAD51D*.

METHODS

Cohort

- 238 women with a personal history of ovarian cancer were found to carry a single PV in *BRIP1*, *RAD51C* or *RAD51D* through clinical testing with a 25-gene panel between September 2013 and July 2016.
- Clinical information was collected from provider-completed test request forms.
- Women identified with PVs in *BRCA1*, *BRCA2*, or the mismatch-repair (MMR) genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*) over the same time period were evaluated for comparison.

Genetic Testing

- The gene panel included *APC*, *ATM*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*,*CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, *MUTYH*, *NBN*, *PALB2*, *PMS2*, *PTEN*, *RAD51C*, *RAD51D*, *SMAD4*, *STK11*, and *TP53*.
- All genes underwent sequencing and large rearrangement analysis, except *EPCAM* (large rearrangement only).
- PVs are those variants that receive a laboratory classification of Deleterious or Suspected Deleterious.

RESULTS

- Table 2 shows that the average age of diagnosis for women with a PV in *BRIP1* (63.7), *RAD51C* (60.7), or *RAD51D* (56.6) was:
  - Similar to the average age of diagnosis for women with a PV in *BRCA2* (59.3).
  - Older than women with a PV in *BRCA1* (53.5) or the MMR genes (45.2 to 51.3).

Table 1. Personal Cancer History of *BRIP1, RAD51C* or *RAD51D* PV Carriers

Gene	Ovarian	Breast + Ovarian
BRIP1	111 (88.1%)	15 (11.9%)
RAD51C	66 (81.5%)	15 (18.5%)
RAD51D	28 (90.3%)	3 (9.7%)
Total	205	33

Note: 12 patients with ovarian cancer and 4 with breast and ovarian cancer had another cancer not listed here.

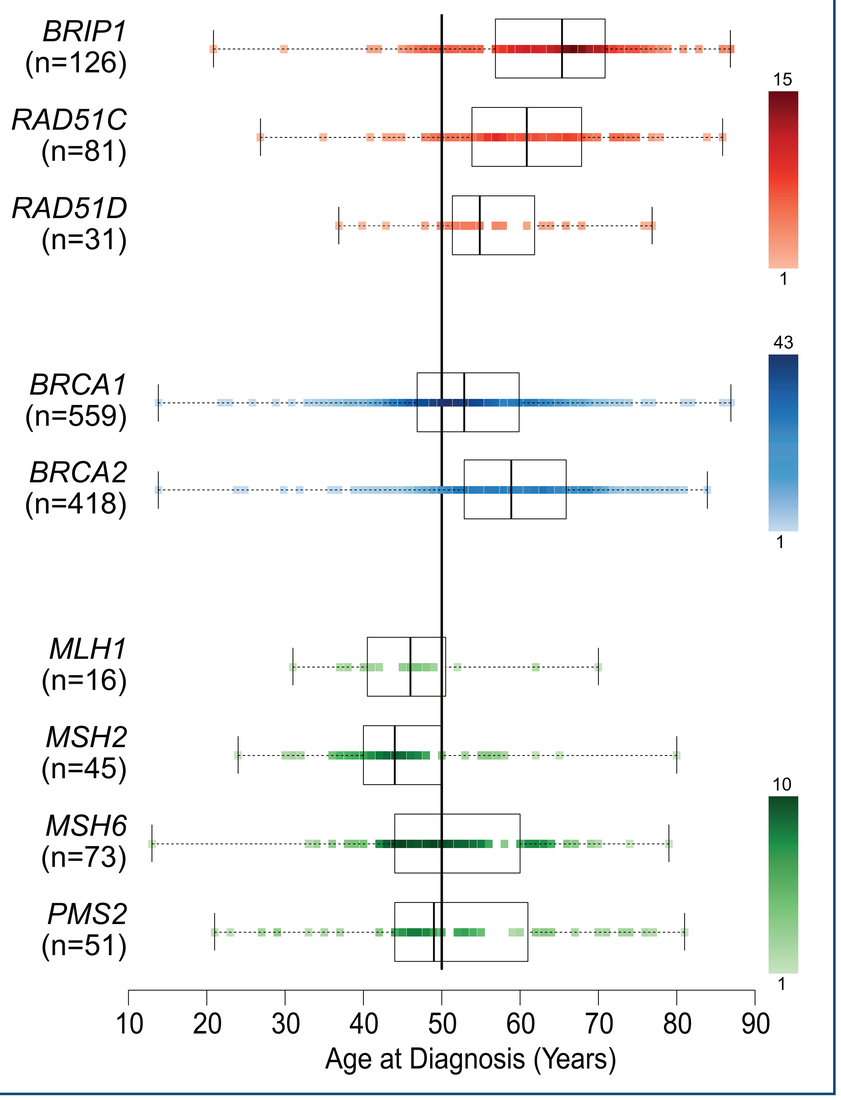
Table 2. Age of Ovarian Cancer Diagnosis

Gene	N	Mean Age (SD)
BRIP1	126	63.7 (11.65)
RAD51C	81	60.7 (10.57)
RAD51D	31	56.6 (9.19)
BRCA1	559	53.5 (9.73)
BRCA2	418	59.3 (10.11)
MLH1	16	47.3 (10.20)
MSH2	45	45.2 (9.89)
MSH6	73	51.3 (10.77)
PMS2	51	50.8 (14.45)
EPCAM	0	—

- The majority of ovarian cancers were diagnosed after the age of 50 among women with a PV in *BRIP1* (85.7%), *RAD51C* (82.7%), or *RAD51D* (77.4%) (Figure 1).

Figure 1. Age of Diagnosis of Ovarian Cancer

The 25–75th percentiles are shown as boxes and a line at age 50 approximates the age of menopause.



CONCLUSIONS

- In this study, we found that the average age of ovarian cancer diagnosis among women with a PV in *BRIP1*, *RAD51C* or *RAD51D* was similar to *BRCA2*.
- Collectively, the data presented here may aid clinical decisions regarding the age at which oophorectomy might be appropriate for women who carry PVs in these 3 genes.
- More research is needed to determine if this management regimen is most beneficial for the patient population in question.

REFERENCES

1. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. V 2.2016. March 15. Available at http://www.nccn.org.

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