Salpingectomy in ovarian cancer prevention

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Discussion

- Feasibility and the role of salpingectomy in women with *BRCA* mutations or other genetic predisposition to ovarian cancers.

Preventing Ovarian Cancer in High-Risk Women

- Around **15-20%** of all ovarian cancers are attributed to inherited *BRCA* mutations.
- The lifetime risk of ovarian cancer is estimated at **45% for *BRCA1*** nutation carriers and **20% for *BRCA2*** mutation carriers.
- Lifetime risk estimates for pathogenic mutations in moderate-risk genes (RAD51C, RAD51D, BRIP1, STK11; Lynch Syndrome genes) range from **5% to 11%**.
- Risk-reducing salpingo-oophorectomy (RRSO) is recommended as standard procedure for decreasing the risk of ovarian cancers.
  - 75% to 96% reduction in the risk of ovarian cancer
  - 35~40 years for *BRCA1* mutation carriers
  - 40~45 years for *BRCA2* mutation carriers
  - 45~50 years for other germline mutations implicated in the carcinogenesis of EOC

Kotsopoulos J, Narod SA. Int J Cancer. 2020;147(5):1245-1251.

Preventing Ovarian Cancer in High-Risk Women

- Removal of the ovaries carries significant side effects, specifically loss of fertility and the premature menopause.
  - Only 60% to 70% of these women undergo RRSO

- **Risk-reducing salpingectomy with delayed oophorectomy (SDO)** has emerged as a potential novel preventive strategy for these patients.

  ① Removal of the fallopian tubes when childbearing is complete (or earlier if assisted reproductive technology is planned)

  ② A delayed oophorectomy at a later age

Is SDO a Better Option?

Kotsopoulos J, Narod SA. Int J Cancer. 2020;147(5):1245-1251.

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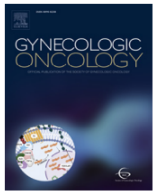

Patient perspectives on risk-reducing salpingectomy with delayed oophorectomy for ovarian cancer risk-reduction: A systematic review of the literature

Table 1
Description of studies reviewed and estimates of RRSDO acceptance.

Author	Setting and population	Participant characteristics Median age (range), race	Design	Key Results
Arts-de Jong et al., 2015	Netherlands BRCA mutation carriers who have already undergone bilateral salpingo-oophorectomy	n = 39 Age: 45 (33–56) Race: 100% White	4 focus groups	44% would have preferred a RRSDO over RRSO if the option were available to them at the time, 44% preferred RRSO, 12% unsure.
Gaba et al., 2021	United Kingdom Adult women with increased ovarian cancer risk and with/without previous RRSO seen at 6 NHS clinics specialized in HBOC & 1 patient support group	n = 683 Age: 45 (19–81) 89% White 11% Non-White	Paper and/or online questionnaire	69% of premenopausal participants who had not undergone RRSO found it acceptable to participate in a study offering RRSDO. 38% of those who had undergone RRSO would have preferrered RRSDO if available at the time, 55% among those who had not undergone RRSO would be interested.
Gaba et al., 2022	United Kingdom Premenopausal BRCA carriers participanting in PROTECTOR trial which allows participants to choose study arm: RRSDO, RSSO, no surgery	n = 24 Age: 39 (34–46) 91.7% White 8.3% Asian	In-depth semi-structured telephone interviews	46% chose RRSDO, 29% chose RRSO, and 25% selected no surgery.
Gellman et al., 2022	United States Patients seen at an academic medical center and with documented deleterious mutation in a gene associated with ovarian cancer	n = 17 Age: 38 (31–46) Race: 100% White	In-depth semi-structured telephone interviews	71% were planning or underwent RRSDO, 23% were planning or underwent RRSO, 6% were undecided.
Holman et al., 2014	United States BRCA mutation carriers who access Facing Our Risk of Cancer Empowered patient advocacy group's social media, newsletter and website	n = 204 Age: 35 (21–53) Race: 90.7% White 3.4% Hispanic 3.9% Other 2% Unkown	Online survey	34% of participants reported definite interest in participating in a study of RRSDO, 35% unsure, 30% not interested in study.
Nebgen et al., 2018	United States BRCA mutation carriers participating in nonrandomized multicenter pilot study of RRSDO vs. RRSO vs. no surgery	n = 43 Age: 38 (32–47) Participant race not reported	Quality of life questionaires administered as part of the pilot study	44% chose RRSDO over RRSO, 28% chose RRSO, and 28% chose no surgery.

RRSO – Risk-reducing salpingo-oophorectomy; RRSDO – Risk-reducing salpingectomy with delayed oophorectomy; NHS—National Health Service; HBOC: hereditary breast and ovarian cancer.

Several studies have evaluated acceptance and surgical decision-making regarding RRSO and SDO among patients with an increased risk of ovarian cancer

Acceptance of SDO ranged from 34% to 71%

Perez L et al. Gynecol Oncol. 2023;173:106-113.

Table 2
Factors that impact patient preferences risk reducing salpingectomy with delayed oophorectomy.

Study	Delay menopause	Preserve fertility	Concerns about sexual dysfunction	Personal history of breast cancer	Family history of breast cancer	Flexible timing of delayed oophorectomy	Avoiding hormone replacement therapy	Oncologic Safety of RRSDO	Potential surgical complications
Arts-de Jong et al. 2015	✓	✓	✓	✓	✓		✓	✓	
Gaba et al. 2021	✓	✓	✓	✓	✓	✓		✓	✓
Gaba et al. 2022	✓	✓		✓	✓	✓	✓	✓	✓
Gellman et al. 2022	✓	✓	✓		✓		✓	✓	
Holman et al. 2014	✓							✓	✓
Nebgen et al. 2018	✓								

Two main factors that impact patient's decision on SDO were delay menopause and concerns of oncologic safety of SDO.

Perez L et al. Gynecol Oncol. 2023;173:106-113.

Trials investigating the impact of SDO over RRSO on ovarian cancer prevention and on QoL

Study	Title	Design
PROTECTOR trial	Preventing Ovarian Cancer through early Excision of Tubes and Late Ovarian Removal	prospective non-randomized
WISP trial	Women Choosing Surgical Prevention	prospective non-randomized
TUBA study	Early salpingectomy (TUbectomy) with delayed oophorectomy to improve quality of life as alternative for risk-reducing salpingo-oophorectomy in BRCA1/2 mutation carriers	prospective non-randomized
SoROCK trial	Non-Inferiority of Salpingectomy to Salpingo-oophorectomy to Reduce the Risk of Ovarian Cancer Among BRCA1 Carriers	prospective non-randomized

Potential barriers to SDO

The need for 2 separate operations	The benefit of oophorectomy extends beyond preventing ovarian cancers
• Increased perioperative risk • Uncertain compliance for the delayed oophorectomy	• Oophorectomy is also associated with **a reduction in all-cause mortality** among women with *BRCA* mutations. • Oophorectomy **prevents death from breast cancer**. It worked for oophorectomies done before a diagnosis of breast cancer and for oophorectomies after a diagnosis of breast cancer.

Discussion-1

- Based on current evidence, could women with *BRCA* mutations be offered bilateral salpingectomy with delayed oophorectomy for ovarian cancer risk reduction?
- From an oncologist's point of view, what are the main concerns regarding the decision making on RRSO or SDO?

Discussion-2

- Regarding the relative low lifetime risk for ovarian cancer, whether salpingectomy alone is a feasible risk-reducing strategy for moderate-risk women?