Risk-reducing salpingo-oophorectomy in patients at high risk of epithelial ovarian and fallopian tube cancer

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Literature review current through: **Sep 2024.**
This topic last updated: **Sep 12, 2024.**

INTRODUCTION

Risk-reducing bilateral salpingo-oophorectomy (rrBSO, also termed risk-reducing salpingo-oophorectomy [rrSO]) is an important option for reducing the risk of developing epithelial ovarian and fallopian tube cancer in patients with a hereditary ovarian cancer syndrome [1]. Risk-reducing surgery includes bilateral removal of the tubes as well as the ovaries because some apparent ovarian cancers are initiated in the fallopian tubes, particularly in patients with pathogenic variants in the breast cancer susceptibility (*BRCA*) genes, *BRCA1* and *BRCA2* [2]. Although rrBSO results in sterility and surgical menopause, alternative preventive and surveillance measures are of limited efficacy in reducing the high rate of cancer mortality in such patients.

Some patients with a hereditary ovarian cancer syndrome are also at risk for other malignancies; thus, decisions regarding cancer risk-reduction strategies must also take into account prevention or surveillance of these other tumors. For example, patients who are carriers of pathogenic variants in the *BRCA* gene are at increased risk for breast and peritoneal cancer, and patients with Lynch syndrome (hereditary nonpolyposis colorectal cancer) are at increased risk for endometrial or colon cancer [3].

This topic will discuss rrBSO as a strategy to prevent ovarian and fallopian tube cancers in patients at high risk for these malignancies. Elective salpingo-oophorectomy at the time of hysterectomy in patients at average risk of ovarian cancer and opportunistic salpingectomy (the removal of the fallopian tubes for primary prevention of epithelial carcinoma of the ovary,

fallopian tube, or peritoneum in a patient undergoing pelvic surgery for another indication) are discussed separately.

- (See "Elective oophorectomy or ovarian conservation at the time of hysterectomy".)
- (See "Opportunistic salpingectomy for ovarian, fallopian tube, and peritoneal carcinoma risk reduction".)

CANDIDATES

rrBSO is reserved for patients at the highest risk of epithelial ovarian and fallopian tube cancer and is consistently recommended in guidelines for patients in the following categories:

- Patients with pathogenic variants in *BRCA1*, with a lifetime risk of ovarian cancer 39 to 59 percent. (See "Cancer risks in BRCA1/2 carriers", section on 'Bilateral salpingo-oophorectomy'.)
- Patients with pathogenic variants in *BRCA2,* with a lifetime risk of ovarian cancer 11 to 20 percent. (See "Cancer risks in BRCA1/2 carriers", section on 'Bilateral salpingo-oophorectomy'.)
- Patients with Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome) have a high risk of ovarian and endometrial cancer; the risk varies and depends on the underlying genetic variant (table 1).
- rrBSO has also been suggested for patients with pathogenic variants in *BRIP1, RAD51C,* and *RAD51D* [4]. The performance of rrBSO in patients carrying other genes associated with an increased risk of developing hereditary ovarian cancer syndrome is more provider and patient dependent. (See "Overview of hereditary breast and ovarian cancer syndromes".)

By comparison, in the general population, the lifetime risk of developing ovarian cancer is 1.5 percent, which is considered average risk. Patients at average risk are not candidates for rrBSO as elective oophorectomy has potential risks. (See "Elective oophorectomy or ovarian conservation at the time of hysterectomy", section on 'Long-term health risks'.)

Some pathogenic variants once thought to be deleterious have been subsequently found not to be associated with increased risk. Thus, if rrBSO is planned based on genetic testing performed more than one year previously, the surgeon should run the genetic variant through ClinVar to ensure that it has not been reclassified from deleterious. This is particularly true for the less common mutations in *BRCA* and the less common gene mutations. ClinVar is an online

aggregator that combines data from genetic testing companies and gives the most current status on mutations. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes", section on 'Criteria for genetic risk evaluation'.)

EFFICACY OF CANCER RISK REDUCTION

rrBSO is the most effective approach to reducing the risk of ovarian and fallopian tube cancer in high-risk patients. When performed before age 50, rrBSO is also associated with a decreased risk for breast cancer in *BRCA* carriers with no prior breast cancer. When performed with hysterectomy, rrBSO reduces the risk of endometrial and ovarian cancer in patients with Lynch syndrome. Data showing the magnitude of risk reduction are presented separately. (See "Cancer risks in BRCA1/2 carriers", section on 'Risk-reducing surgery'.)

PREOPERATIVE EVALUATION AND PREPARATION

Counseling and consent — Patient counseling should address the following issues:

- The patient's risk for developing cancer and the expected reduction in risk as a result of the procedure. (See "Cancer risks in BRCA1/2 carriers", section on 'Risk-reducing surgery'.)
- Alternatives to rrBSO for cancer risk reduction, although these are less effective. (See 'Less effective alternatives to rrBSO' below.)
- Consequences of rrBSO other than cancer risk reduction, including infertility and premature menopause. In particular, issues relating to menopause and its treatment should be reviewed (eg, vaginal dryness, changes in libido and sexual function, sleep disturbances, hot flashes, osteoporosis, mood changes, and risk of coronary heart disease) [5,6]. (See "Clinical manifestations and diagnosis of menopause" and "Treatment of menopausal symptoms with hormone therapy".)
- The possibility of future in vitro fertilization. Patients should delay rrBSO until after completion of childbearing, but some patients who are considering rrBSO because of advancing age may not be able to complete childbearing by age 35 to 40 years. These patients can be counseled about alternative reproductive options, which include oocyte and embryo cryopreservation. (See "Fertility and reproductive hormone preservation: Overview of care prior to gonadotoxic therapy or surgery".)

- Potential findings at surgery. The chance of detecting occult malignancy either at the time of surgery or in the final pathology report ranges widely. For example, in the author's institution, the rate of occult malignancy at the time of rrBSO is <3 percent; however, reports in the literature range from 0.6 to 18.5 percent [7-11]. The wide range likely reflects the various techniques and definitions used when evaluating pathology specimens and/or the differences in patient age when the operation is performed [12]. For example, in a study of older (≥45 years of age) and younger *BRCA1* carriers undergoing rrBSO, the frequency of occult malignancy was higher in older patients (12.2 versus 3.6 percent) [10].

  Thus, it is important to counsel patients preoperatively about the potential need for additional surgery and to obtain informed consent for this surgery. Most will give consent for additional surgery at the time of the initial operation, although some patients prefer a two-stage approach.

- Limitations of surgery. Patients at high risk for ovarian cancer may develop primary peritoneal carcinoma and remain at risk for this cancer after rrBSO. The risk appears to be highest in patients with pathogenic variants in *BRCA1* or *BRCA2* who demonstrate serous tubal intraepithelial carcinoma lesions at rrBSO [13]. (See "Cancer risks in BRCA1/2 carriers", section on 'Bilateral salpingo-oophorectomy'.)

Timing — Generally, rrBSO should be performed as soon as childbearing is complete or by age 35 to 40 years since the benefit diminishes with age [14,15]. Timing of rrBSO requires balancing the procedure-related consequences of infertility and premature menopause against the risk of ovarian and fallopian tube cancer, which is uncommon before age 40 and rare before age 30 [16,17].

The average age of ovarian cancer diagnosis varies with type of mutation. Patients who carry *BRCA1* mutations have a significant rise in ovarian cancer risk beginning at 35 years of age, with 2 to 3 percent of these patients developing ovarian cancer by age 40 years; the average age at diagnosis is 50 years [17-23]. *BRCA2* mutation carriers reach a 2 to 3 percent incidence of ovarian cancer a decade later, by age 50 years; the average age at diagnosis is 60 years, similar to the general population. Based upon this difference in the likely age of onset of ovarian cancer, *BRCA2* carriers may wish to delay risk-reducing surgery, but by doing so, they would not benefit from the reduced risk of breast cancer afforded by salpingo-oophorectomy [24]. Gains in life expectancy after rrBSO have been estimated using decision analysis [14,25]. Life expectancy gains declined with age at the time of surgery and were minimal for 60 year-old patients, although there was little loss in life expectancy if the surgery was performed at age 40 rather than age 30.

In one prospective study including 357 patients (mean age 44 years) diagnosed with a *BRCA1/2* pathogenic variant, 79 percent underwent an rrBSO procedure; mean time from genetic testing to surgery was 29.5 months and almost one-third of patients had the procedure within six months [26,27]. Patients diagnosed with *BRCA1/2* at age <30 compared with ≥30 years had the lowest rates of rrBSO.

Patients with Lynch syndrome typically develop ovarian cancer between the ages of 43 and 48 years (see "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Screening and prevention of endometrial and ovarian cancer", section on 'Risk for ovarian cancer'). In general, we recommend rrBSO in the mid-40s for patients with Lynch syndrome. There is some variability based on the type of mutation, but in general, we tend to manage these patients much like *BRCA2* carriers.

Preoperative evaluation — Prior to rrBSO, patients should undergo screening for an ovarian malignancy with pelvic sonography and measurement of serum cancer antigen 125 (CA 125). A baseline CA 125 level is also useful because the level is followed postoperatively for surveillance for development of peritoneal cancer. However, clinicians and patients should not be falsely reassured by negative screening test results. (See 'Intensive screening to detect early stage disease' below and "Screening for ovarian cancer", section on 'Cancer antigen 125 (CA 125)' and "Screening for ovarian cancer", section on 'Transvaginal ultrasound (TVUS)'.)

Detection of a possible ovarian malignancy could change the scope of the preoperative evaluation and the planned procedure. For example, preoperative evaluation for metastatic disease might be indicated and consent and surgical preparation for complete surgical staging (table 2) would be indicated if an ovarian, fallopian tube, or peritoneal cancer is confirmed at surgery.

PROCEDURE

Surgical approach — The surgical route may be by laparoscopy or laparotomy. Laparoscopy is generally preferable since it is associated with less morbidity and allows for an outpatient procedure. (See "Complications of laparoscopic surgery".)

BSO versus salpingectomy alone — The minimum operation required for risk reduction for ovarian and fallopian tube cancer is a bilateral salpingo-oophorectomy (BSO) since "ovarian" epithelial neoplasms have three potential sites of origin: ovary, fallopian tube, and other müllerian epithelial sites in the pelvis.

Studies of rrBSO in patients with pathogenic variants of *BRCA* genes have consistently noted occult primary fallopian tube cancers in surgical specimens [16,28-40]. The finding of early fallopian tube cancers in these patients as well as the potential role of endosalpingiosis in female pelvic serous tumors has raised the possibility of performing risk-reducing salpingectomy alone, particularly for patients who wish to preserve fertility. Two approaches that have been proposed, but remain investigational, are bilateral salpingectomy alone and bilateral salpingectomy followed by delayed oophorectomy, thereby avoiding premature menopause and preserving oocytes for use with assisted reproductive technology [41].

At least two cases of ovarian cancer have been reported in this patient population [42,43]. In one case, the patient was a *BRCA1* carrier who developed stage IV ovarian cancer four years after risk-reducing bilateral salpingectomy without oophorectomy [44]. Disease was advanced at diagnosis despite periodic surveillance with clinical examinations and cancer antigen 125 (CA 125) levels. Clinical trials evaluating salpingectomy with delayed oophorectomy in high-risk patients are ongoing [45].

For patients with pathogenic variants of *BRCA* genes, not performing or delaying oophorectomy is likely to diminish or eliminate the possible prophylactic effect on breast cancer associated with oophorectomy (see "Cancer risks in BRCA1/2 carriers", section on 'Risk-reducing surgery'). Furthermore, if oophorectomy is not performed, it is unclear whether the surgeon can remove the entire fimbriated end of the fallopian tube, which may be the most likely site of tubal malignancy [16,33]. Moreover, the surface of the ovary and mesovarium may contain tubal epithelium, which is a potential site of origin of epithelial ovarian carcinoma.

"Radical salpingectomy," in which the adjacent ovarian cortex is resected in continuity with the tube, has been proposed to overcome the limitations of salpingectomy without oophorectomy. The radical procedure and use of bipolar cautery devices to perform salpingectomy may cause unintended damage to ovarian cortex or collateral vessels, thus reducing ovarian function and the potential benefits of preserving the ovaries.

Abdominopelvic evaluation — When rrBSO is performed, a methodical survey should be conducted of the abdomen (diaphragm, liver, omentum, bowel, paracolic gutters, appendix), pelvis (ovaries, fallopian tubes, uterus, posterior cul-de-sac), and the entire peritoneum. Some surgeons perform an omental biopsy and cytologic smear of the diaphragm [42,46]. Suspicious areas should be biopsied with liberal use of frozen section [47].

Peritoneal lavage is also performed, although the sensitivity, specificity, and prognostic value of positive lavage cytology have not been determined. Multiple small series of patients at high risk for ovarian cancer undergoing rrBSO or hysterectomy reported finding several patients with

occult malignancy in the ovary or fallopian tube, and most had malignant cells identified in lavage fluid [31,33-36,48]. One patient had malignant cells confined to the peritoneal lavage specimen with no evidence of carcinoma in the uterus, tubes, or ovaries. No long-term follow-up data are available.

If frozen section reveals carcinoma, a staging procedure is performed if the patient has consented (table 2). Otherwise, the procedure is terminated, the findings are discussed with the patient postoperatively, and then another procedure is scheduled for surgical staging. (See "Epithelial carcinoma of the ovary, fallopian tube, and peritoneum: Surgical staging".)

Scope of resection

- All ovarian tissue should be removed [49].
- If adhesions between the ovary and other peritoneal structures are present, the entire adhesion should be resected with the ovary to ensure that no residual ovarian cells remain attached to the peritoneal surface [50].
- The retroperitoneal space should be entered and the ovarian pedicle clamped and cut at least 2 cm proximal to the ovary, and preferably at the pelvic brim, to avoid leaving any ovarian tissue behind [46,51]. The pelvic peritoneum should be opened to visualize the ureter and isolate the infundibulopelvic ligament before transection. Complications are infrequent in experienced hands [29]. (See "Oophorectomy and ovarian cystectomy".)
- As much of the fallopian tube as possible should be removed. Complete fimbrial resection is important, but complete cornual resection to remove the intramural (interstitial) portion of the tube does not appear to be necessary, particularly during laparoscopic procedures. In a series of *BRCA* carriers undergoing rrBSO, six patients had an occult malignancy in the surgical specimen, and five of these six malignancies were in the fimbrial portion of the fallopian tube [16].

  Although the interstitial portion of the fallopian tube is typically left behind after rrBSO, we are not aware of any reports of cases of malignant transformation in the tubal remnant after this type of surgery [52]. A clinicopathologic study of 105 fallopian tube cancers found that none were interstitial, 92 percent were situated within the ampullary and isthmic portion, and 8 percent were confined to the infundibulum and fimbriae [53].

Should concurrent hysterectomy be performed? — Risk-reducing hysterectomy may be beneficial in some groups of patients:

- **Patients with Lynch syndrome** – Endometrial cancer is the second most common malignancy (after colorectal cancer) in patients with Lynch syndrome. The lifetime risk of developing endometrial cancer varies by genotype (ie, *MLH1, MSH2, MSH6, PMS2*) (table 1). Thus, total hysterectomy in addition to rrBSO is the appropriate recommendation in patients with this disorder who desire surgical risk reduction. (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Screening and prevention of endometrial and ovarian cancer", section on 'Strategies for cancer risk reduction'.)

- **Patients planning to take** tamoxifen – Patients with *BRCA1* and *BRCA2* pathogenic variants may opt to take tamoxifen, a selective estrogen receptor modulator, for chemoprophylaxis of breast cancer. Tamoxifen use is associated with an increased risk for endometrial cancer. Thus, patients planning to use tamoxifen after rrBSO may consider risk-reducing hysterectomy at the time of ovarian extirpation [15]. (See "Endometrial carcinoma: Epidemiology, risk factors, and prevention", section on 'Tamoxifen'.)

- **Patients who wish to take unopposed estrogen therapy for relief of menopausal symptoms** – After hysterectomy, therapy with unopposed estrogen can be given without endometrial monitoring or a concurrent progestin since endometrial carcinoma is not a concern. Estrogen alone appears to be associated with a lower breast cancer risk than combined (estrogen with progestin) hormonal therapy. These data are reviewed in detail separately. (See "Cancer risks in BRCA1/2 carriers", section on 'Hormone therapy for those undergoing rrBSO' and "Menopausal hormone therapy and the risk of breast cancer".)

Data regarding endometrial cancer risk in patients who are carriers of pathogenic *BRCA* variants are conflicting; any increase in cancer risk appears to be small [54,55]. We feel performance of a risk-reducing hysterectomy along with rrBSO in *BRCA* carriers is discretionary. (See "Cancer risks in BRCA1/2 carriers", section on 'Other gynecologic malignancies'.)

Following rrBSO, few patients (<10 percent in one series [56]) require hysterectomy for standard indications (eg, symptomatic fibroids, prolapse); thus, there is no compelling reason to perform concurrent hysterectomy to avoid future surgery.

The disadvantage of adding hysterectomy to rrBSO is that it increases the morbidity of the procedure and may require a short hospital stay. There is no strong evidence that incidental hysterectomy either protects against or increases the risk for future urinary incontinence or pelvic organ prolapse. (See "Hysterectomy: Laparoscopic".)

Pathology evaluation — Multiple 2 to 3 millimeter longitudinal sections of the resected ovaries and fallopian tubes should be examined microscopically for occult carcinoma using a protocol

specific for patients at high risk of an occult malignancy [15,16,31,34]. We use the Sectioning and Extensively Examining the FIMbria (SEE-FIM) protocol [16].

FOLLOW-UP

Occult malignancy on pathology — While uncommon, occult malignancy may be found on final pathologic examination of the rrBSO specimen (see 'Counseling and consent' above). These patients are counseled about the implications of the findings and appropriate surgical and medical treatment. (See "Adjuvant therapy of early-stage (stage I and II) epithelial ovarian, fallopian tube, or peritoneal cancer" and "Management of ovarian cancer associated with BRCA and other genetic mutations".)

There is no consensus regarding how to manage patients with or without pathogenic *BRCA* variants in whom serous tubal intraepithelial carcinoma (STIC) is discovered at rrBSO. Adjuvant chemotherapy has been proposed for STIC without concurrent invasive carcinoma found at rrBSO, but there are insufficient data to determine the efficacy of this approach and whether the benefit outweighs the risks of therapy. Data regarding use of chemotherapy in patients with STIC are limited to small case reports or case series (table 3). To date, across a range of study designs, a total of 54 patients with STIC have been observed for a period ranging from 7 to 150 months [34,35,57-62]. All patients had peritoneal washings, of which 16 were positive. Chemotherapy was given in 12 cases. Only two recurrences (after 43 and 48 months) have been documented, and these were in patients with negative peritoneal washings who did not receive chemotherapy [60,62]. Thus, it is unclear how adjuvant chemotherapy impacts the risk of progression of STIC to invasive carcinoma.

Although the available data do not support routine administration of adjuvant chemotherapy in patients with STIC alone with either positive or negative washings [35], for each patient, a careful clinical risk assessment should be made, and the approach should be individualized. If STIC is found and the pelvic washings are negative, conservative management is the usual choice. (See 'Surveillance for peritoneal cancer' below.)

Surveillance for peritoneal cancer — Patients who have undergone rrBSO are at risk of developing serous carcinoma of the peritoneum (incidence 1.7 percent in one prospective study [50]). There are no high-quality data regarding the optimal methods of surveillance for peritoneal cancer following rrBSO. In our practice, we follow patients with an annual pelvic examination and serum CA 125 for 10 years. The interpretation and diagnostic performance of this test are reviewed separately. (See "Adnexal mass: Role of serum biomarkers in diagnosing

epithelial carcinoma of the ovary, fallopian tube, or peritoneum", section on 'Cancer antigen 125'.)

Management of premature menopause — Patients who undergo rrBSO differ in several important ways from the general menopausal population.

- They undergo surgical rather than natural menopause. As a result, ovarian hormone levels drop abruptly, and all hormone production ceases. By contrast, in natural menopause, hormone levels decrease gradually, and the ovaries continue to produce some hormones (eg, androgens).

- They are typically younger than the average age of menopause (average age is 51 years old). Thus, they will be exposed to the detrimental effects of hypoestrogenism (eg, effects on bone density, cardiovascular health) for a longer period of time. (See "Elective oophorectomy or ovarian conservation at the time of hysterectomy", section on 'Consequences of elective oophorectomy'.)

Menopausal symptoms or preventive care can be managed with hormonal and/or nonhormonal approaches, which are discussed in detail separately.

- (See "Cancer risks in BRCA1/2 carriers", section on 'Hormone therapy for those undergoing rrBSO'.)
- (See "Menopausal hot flashes", section on 'Nonhormonal pharmacotherapy'.)
- (See "Genitourinary syndrome of menopause (vulvovaginal atrophy): Treatment", section on 'Initial therapy with moisturizers and lubricants'.)

LESS EFFECTIVE ALTERNATIVES TO rrBSO

rrBSO is the most effective option for reducing the risk of ovarian and fallopian tube cancer and is the approach that we recommend. Approximately 70 percent of patients who are *BRCA1* and *BRCA2* carriers undergo this procedure [63]. Other options are discussed below.

Intensive screening to detect early stage disease — Some expert groups have recommended screening with pelvic sonography plus cancer antigen 125 assays every six months starting at age 35 years or five to ten years earlier than the earliest age of first diagnosis of ovarian cancer in the family [64]. If screening leads to detection and treatment of early stage disease, overall survival is good (table 4).

However, screening has not been found to improve survival in patients at high risk for ovarian cancer, and clinicians and patients should not be falsely reassured by negative screening test

results [65]. Most studies show that, even with intensive screening, ovarian cancers are usually diagnosed at an advanced stage [66-68]. (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Screening and prevention of endometrial and ovarian cancer", section on 'Ovarian cancer surveillance' and "Cancer risks in BRCA1/2 carriers", section on 'Ovarian cancer screening'.)

Chemoprevention — Use of oral contraceptives has been associated with a reduced risk of ovarian cancer in patients with pathogenic variants of *BRCA1* and *BRCA2* and a reduction in fallopian tube cancer in the general population. These data are discussed separately. (See "Cancer risks in BRCA1/2 carriers", section on 'Contraceptives for ovarian cancer risk reduction'.)

Hysterectomy and tubal ligation — Both hysterectomy and tubal ligation have been associated with a decrease in ovarian cancer risk in the general population but have not been evaluated in high-risk populations. We believe that these procedures are not appropriate for risk-reducing surgery in patients at high risk for ovarian cancer since the ovaries and tubes are not removed. (See "Epithelial carcinoma of the ovary, fallopian tube, and peritoneum: Incidence and risk factors", section on 'Protective factors'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hereditary breast and ovarian cancer".)

SUMMARY AND RECOMMENDATIONS

- **Definition** – Risk-reducing bilateral salpingo-oophorectomy (rrBSO, also termed risk-reducing salpingo-oophorectomy [rrSO]) is the removal of both ovaries and both fallopian tubes in patients at high risk for epithelial ovarian and fallopian tube cancer, such as those with pathogenic variants in *BRCA1* and *BRCA2* or Lynch syndrome; some less common mutations include *BRIP1, RAD51C,* and *RAD51D*. (See 'Introduction' above and 'Candidates' above.)

- **Efficacy** – rrBSO is the most effective approach to reducing the risk of ovarian and fallopian tube cancer in high-risk patients. When performed before age 50, rrBSO is also associated with a decreased risk for breast cancer in *BRCA* carriers with no prior breast cancer. When performed with hysterectomy, rrBSO reduces the risk of endometrial and

ovarian cancer in patients with Lynch syndrome. (See 'Efficacy of cancer risk reduction' above.)

- **Counseling** – Patient counseling should address the following (see 'Counseling and consent' above):
  - Other consequences of rrBSO, including infertility and premature menopause.
  - An approximate 2 percent chance of developing primary peritoneal carcinoma; this risk remains even after rrBSO.
  - A 4 to 8 percent risk of having an unsuspected malignancy detected either at the time of surgery or in the final pathology report.
- **Timing** – Generally, rrBSO should be performed as soon as childbearing is complete or by age 35 to 40 years since the benefit diminishes with age. (See 'Timing' above.)
- **Preoperative evaluation** – Prior to rrBSO, patients should undergo screening for an ovarian malignancy with pelvic sonography and measurement of serum cancer antigen 125 (CA 125). (See 'Preoperative evaluation' above.)
- **Role of salpingectomy alone** – rrBSO is the standard of care, but risk-reducing salpingectomy is an investigational alternative surgical approach that has been proposed. Techniques include bilateral salpingectomy alone and bilateral salpingectomy followed by delayed oophorectomy, thereby avoiding premature menopause and preserving oocytes for use with assisted reproductive technology. (See 'BSO versus salpingectomy alone' above.)
- **Role concurrent hysterectomy** – Candidates for concurrent hysterectomy include patients with Lynch syndrome, patients with *BRCA1* and *BRCA2* pathogenic variants who opt to take tamoxifen for chemoprophylaxis of breast cancer, and those who wish to take unopposed estrogen therapy for treatment of menopausal symptoms. (See 'Should concurrent hysterectomy be performed?' above.)
- **Follow-up**
  - Patients with occult malignancy on histopathology are counseled about the implications of the findings and appropriate surgical and medical treatment. (See 'Occult malignancy on pathology' above.)

- We follow patients with no gross or occult malignancy at rrBSO with an annual pelvic examination and serum CA 125 and offer treatment for menopausal symptoms. (See 'Surveillance for peritoneal cancer' above and 'Management of premature menopause' above.)

ACKNOWLEDGMENTS

The UpToDate editorial staff acknowledges Michael G Muto, MD, who contributed to earlier versions of this topic review.

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Topic 3250 Version 58.0

GRAPHICS

Lifetime cancer risk related to Lynch genotypes

Cancer site	MLH1		MSH2*		MSH6		PMS2	
	Female	Male	Female	Male	Female	Male	Female	Male
Any Lynch cancer	**80.2%**	**68.5%**	**83.4%**	**80.5%**	**55.2%**	**28.5%**	**40.1%**	**57.3%**
Colorectal	48.3%	56.0%	42.6%	55.8%	17.3%	16.4%	8.5%	32.8%
Endometrial	37.2%	–	44.1%	–	45.7%	–	21.2%	–
Gastric	4.3%	8.9%	4.0%	8.3%	0.7%	0.7%	¶	2.7%
Ovarian	8.0%	–	13.4%	–	6.3%	–	2.5%	–
Ureter/kidney	2.9%	4.5%	19.5%	15.8%	3.9%	3.3%	¶	¶
Bladder	4.8%	5.6%	9.4%	13.1%	2.6%	9.0%	¶	¶
Prostate	–	15.6%	–	24.0%	–	7.0%	–	3.3%
Breast[Δ]	12.4%	–	15.5%	–	15.1%	–	12.4%	–
Brain	1.4%	0.6%	2.2%	6.6%	1.2%	0.8%	¶	¶
Small bowel	4.5%	8.3%	3.7%	7.0%	0.6%	2.8%	2.1%	3.3%
Pancreas	3.7%	3.1%	3.5%	3.3%	2.2%	1.2%	¶	¶
Bile duct/gallbladder	1.5%	4.0%	2.4%	4.6%	¶	¶	¶	¶

This table includes cumulative incidences of cancer in respective organs for males and females at 75 years of age.

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* Cancer risks in individuals with a pathogenic *EPCAM* variant are similar to those with a pathogenic *MSH2* variant.

¶ Data are insufficient to make a determination.

Δ There is ongoing debate as to whether breast cancer is a Lynch syndrome-associated cancer.

Data from: Dominguez-Valentin M, Haupt S, Seppälä TT, et al. Mortality by age, gene and gender in carriers of pathogenic mismatch repair gene variants receiving surveillance for early cancer diagnosis and treatment: A report from the prospective Lynch syndrome database. EClinicalMedicine 2023; 58:101909.

Graphic 52285 Version 12.0

Steps in staging ovarian cancer

1. Obtain any free fluid for cytologic evaluation.
2. If no free fluid is present, obtain washings by instilling saline and recovering the fluid. The fluid should irrigate the cul-de-sac, paracolic gutters, and area beneath each diaphragm.
3. Systematically explore all intraabdominal organs and surfaces: Bowel, liver, gallbladder, diaphragms, mesentery, omentum, and the entire peritoneum should be visualized and palpated, as indicated.
4. Suspicious areas or adhesions should be biopsied. If there are no suspicious areas, multiple biopsies should be obtained from the peritoneum of the cul-de-sac, paracolic gutters, bladder, diaphragm, and intestinal mesentery when the disease appears confined to the ovary. These biopsies are not needed i the patient has advanced disease.
5. The omentum should be resected from the transverse colon.
6. The retroperitoneum should be explored to evaluate pelvic nodes. Suspicious nodes should be removed and sent for frozen section examination.
7. The paraaortic nodes should be exposed and enlarged nodes removed. Nodes superior to the inferior mesenteric artery should also be resected.
8. In the absence of suspicious nodes, pelvic and paraaortic nodes should still be sampled to exclude the possibility of microscopic stage III disease.
9. A total abdominal hysterectomy and bilateral salpingo-oophorectomy is performed. (Fertility-conserving surgery may be an option for some patients.)

Graphic 75194 Version 7.0

Serous tubal intraepithelial neoplasm (STIC): Follow-up of cases

Study	Number of patients with STIC	Positive washings	Chemotherapy	Recurrence	Follow-up (in months
Paley et al 2001[1]	2	2 of 2	1	0	36 to 48
Agoff et al 2002/2004[2,3]	3	1 of 3	2	0	36
Leeper et al 2002[4]	2	1 of 2	2	0	8 to 17
Manchanda et al 2011/2012[5,6]	7	3 of 7	0	0	7 to 48
Powell et al 2013[7]	17	3 of 17	4	1 (43 months)	40 to 150
Wethington et al 2013[8]	12	1 of 12	0	0	16 to 44
Conner et al 2014[9]	11	5 of 11	3	1 (48 months)	12 to 96

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Graphic 96540 Version 2.0

Carcinoma of the ovary: Five-year survival, United States 2007-2013

Stage*	Five-year survival (%)
I	89
II	71
III	41
IV	20

* American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 6th edition.

Adapted from: Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin 2018; 68:284.

Graphic 134243 Version 1.0

Contributor Disclosures

Michael G Muto, MD No relevant financial relationship(s) with ineligible companies to disclose. **Barbara Goff, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Alana Chakrabarti, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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