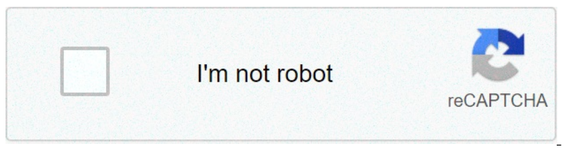

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Risk reducing bso

Key findings Hereditary breast and ovarian cancer (HBOC) syndrome, the most common genetic syndrome linked to ovarian cancer, is most frequently associated with a mutation in BRCA1 or BRCA2 genes Bilateral salpingo-oophorectomy (BSO) is the standard surgical prophylaxis for patients with HBOC syndrome BRCA2 mutation carriers are at lower lifetime risk of ovarian cancer than BRCA1 mutation carriers and can defer BSO to a later age. BRCA1 mutation carriers should undergo BSO directly after childbearing is completed Women with Lynch syndrome have a 24% to 51% lifetime risk of endometrial cancer, depending on the mutation type The standard risk-reducing surgery for Lynch-associated gynecologic cancers is total hysterectomy with or without BSO or bilateral salpingectomy, which should be performed directly after childbearing is completed Certain inherited germline mutations dramatically increase the risk of ovarian or endometrial cancer. For the small number of women who have these mutations, prophylactic surgery has great potential to reduce the risk of cancer. In the Journal of Surgical Oncology, OB/GYN resident Alexandra S. Bercow, MD, and Eric L. Eisenhauer, MD, chief of the Division of Gynecologic Oncology in the Department of Obstetrics and Gynecology at Massachusetts General Hospital, review how women with hereditary breast and ovarian cancer (HBOC) syndrome and Lynch syndrome can reduce their risk of ovarian and endometrial cancer through surgery. HBOC Syndrome HBOC syndrome, the most common genetic syndrome linked to ovarian cancer, is most frequently associated with mutations in the BRCA1 and BRCA2 tumor suppressor genes. The lifetime risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers is 44% and 17%, respectively, compared with 1.3% in the general population. HBOC syndrome can also be associated with germline mutations in a number of other homologous recombination repair genes. Peutz-Jeghers syndrome, which results from mutations in the STK11 gene, has been associated with a 21% lifetime risk of ovarian cancer, which is usually diagnosed in young adulthood or even childhood. Screening Before undergoing BRCA testing, women who have a significant family history of breast or ovarian cancer should consult a genetic counselor for formal risk assessment. The United States Preventive Services Task Force, the American College of Medical Genetics and Genomics and the National Comprehensive Cancer Network have published guidelines about when to refer to a genetic counselor. Risk-reducing Surgery Bilateral salpingo-oophorectomy (BSO) is the standard surgical prophylaxis for patients with HBOC syndrome. It has been linked to significantly improved cancer-specific mortality for ovarian, fallopian tube, peritoneal and breast cancers, as well as improved all-cause mortality in BRCA mutation carriers. Many women with BRCA mutations wish to delay BSO until they complete childbearing. BRCA2 mutation carriers are at lower lifetime risk of ovarian cancer than BRCA1 mutation carriers and are more likely to be diagnosed later in life (at average age 60 vs. age 35 for BRCA1 carriers). Therefore, they may elect to defer BSO to a later age. However, they must be counseled that they might not receive the benefit of decreased breast cancer risk. The Society of Gynecologic Oncology (SGO) recommends that if a BRCA mutation carrier refuses BSO, she should be offered bilateral salpingectomy with delayed oophorectomy, with the caution that it does not decrease the risk of primary ovarian cancer or breast cancer. Unfortunately, annual monitoring with pelvic ultrasound and CA125 levels have not been shown to reduce cancer mortality in this high-risk population. Lynch Syndrome Patients with Lynch syndrome are carriers of mutations in one of four tumor suppressor genes: MLH1, MSH2, MSH6 or PMS2. These genes identify base-pair mismatches during DNA synthesis and repair them. Lynch syndrome was formerly known as hereditary nonpolyposis colorectal cancer. However, women with Lynch syndrome also have a 24% to 51% lifetime risk of endometrial cancer, depending on mutation type, compared with 2.9% in the general population. The average age at diagnosis of endometrial cancer is 47 to 51 years in Lynch syndrome compared with age 60 for average-risk women. Lynch syndrome is also associated with increased risk of other malignancies, including colon, urothelial, gastric, small-bowel, pancreatic, hepatobiliary and brain cancer. Screening Screening for Lynch syndrome should be done according to the revised Amsterdam criteria published in the Journal of Medical Genetics. The SGO incorporates those criteria in its guidelines on cancer risk assessment, adding that pathologic specimens from all women diagnosed with endometrial cancer should be tested for DNA mismatch repair mutations. Risk-reducing Surgery The standard risk-reducing surgery for Lynch-associated gynecologic cancers is total hysterectomy with or without BSO or bilateral salpingectomy. In the largest study to date, led by researchers at the University of Texas M.D. Anderson Cancer Center, prophylactic surgery was associated with a significantly lower risk of both endometrial cancer and ovarian cancer. Because of the younger ages at which endometrial and ovarian cancer are diagnosed in women with Lynch syndrome, prophylactic surgery should be performed directly after completion of childbearing. Patient Counseling About BSO BSO is generally performed laparoscopically and is considered a low-risk procedure, especially if performed at a high-volume institution. However, there is a 4% to 8% chance of discovering an occult malignancy at the time of BSO or on final pathology. Patients should be consented for more extensive surgery if metastatic disease is found and made aware that a second surgery may be necessary if final pathology shows a malignancy. Women should also be counseled that BSO will result in surgical menopause. Non-hormonal agents should be used as a first-line therapy. Unlike BRCA mutations, Lynch syndrome does not carry an increased risk of breast cancer, so the theoretical risk from estrogen-progesterone hormone replacement therapy is low. 44% lifetime risk of ovarian cancer in BRCA1 mutation carriers 17% lifetime risk of ovarian cancer in BRCA2 mutation carriers view original journal article Subscription may be required Journal of Surgical Oncology Journal Article Published: July 29, 2019 Refer a patient to the Mass General Cancer Center Learn more about OB/GYN research at Mass General My colleagues and I recently published a summary of our Society of Gynecologic Oncologists' recommendations on Prophylactic and Risk-Reducing Bilateral Salpingo-oophorectomy (BSO) in the September issue of Obstetrics & Gynecology.We reaffirmed the recommendation that women who are at high risk for ovarian cancer based on the identification that they carry a BRCA1 or BRCA2 mutation should undergo a risk-reducing BSO after completing childbearing, as its value is well documented. These operations are associated with a substantial reduction in the mortality from ovarian and fallopian tube cancers, and a reduction in the mortality from breast cancer.Women with a strong family history who are untested or who test negative may be at higher-than-average risk for ovarian cancer. Because there are no effective ovarian cancer screening tools at present, prophylactic BSO is also indicated in these women at higher-than-average risk.For premenopausal and perimenopausal women at average risk of ovarian cancer who are undergoing a hysterectomy for benign conditions, the decision to also perform a BSO should be individualized after appropriate informed consent. There is a plausible increased risk of several important negative outcomes after prophylactic BSO, especially an increase in mortality from cardiovascular disease and an increase in neurologic diseases. These are dependent on the age at BSO. Therefore, many women in this category might choose to preserve their ovaries as the benefit of this might substantially outweigh the risk.Physicians should thoroughly discuss these issues with their patients who might be planning to undergo surgery under these circumstances. The prevalence of BSO in the U.S. also underscores the necessity of future research.Please consult the full report for detailed information. Sign in to receive recommendations (Learn more) Doctors call removing both ovaries and the fallopian tubes bilateral salpingo-oophorectomy (BSO). When a woman with no known ovary or fallopian tube problems has the procedure to reduce her risk of ovarian and breast cancer, it's called prophylactic BSO.New guidelines on prophylactic BSO were developed by the Society of Gynecologic Oncologists (SGO). The guidelines address the role prophylactic BSO can play in reducing the risk of both ovarian and breast cancer.Most inherited cases of breast and ovarian cancer are associated with mutations in two genes: BRCA1 (BReast CAncer gene one) and BRCA2 (BReast CAncer gene two). BRCA1 and BRCA2 genetic mutations are found in 5% to 10% of all breast cancer cases in the United States. Women with a BRCA1 or BRCA2 mutation have up to a 72% risk of developing breast cancer by age 80. If breast cancer already has been diagnosed, the risk of recurrence (the cancer coming back) is also much higher than average. Women with a BRCA1 or BRCA2 genetic mutation also have a much higher-than-average risk of ovarian cancer -- from 17% to 44%.To reduce future risk of ovarian and breast cancer, SGO guidelines recommend that: Women at high risk for developing breast and ovarian cancer because they have an abnormal BRCA1 or BRCA2 gene should have prophylactic BSO to reduce their risk after they're done having children. Women who have a strong family history of ovarian and/or breast cancer in first-degree relatives (mother, sister, aunt) but who don't have an abnormal BRCA1 or BRCA2 gene (or haven't been tested) should assume they have a higher-than-average risk of ovarian and breast cancer and should have prophylactic BSO to reduce their risk after they're done having children. Women with an average risk of ovarian cancer shouldn't have prophylactic BSO routinely and should carefully weigh the pros and cons of prophylactic BSO if they're considering the surgery. Prophylactic BSO in a woman with an abnormal BRCA1 or BRCA2 gene can: reduce her risk of BRCA-related ovarian cancer by 96% reduce her risk of breast cancer by 50% to 80% (for premenopausal women) significantly reduce her risk of breast cancer coming back if she's been diagnosed Women with a strong family history of ovarian and/or breast cancer in first-degree relatives but who don't have an abnormal BRCA1 or BRCA2 gene may have a different abnormal gene that's not routinely tested for or recognized. This other abnormal gene may increase ovarian and breast cancer risk. So the guidelines recommend that women with a strong family history without an abnormal BRCA1 or BRCA2 gene have prophylactic BSO to reduce their cancer risk once they're done having children.A woman with average ovarian cancer risk might consider prophylactic BSO if she is having a hysterectomy (removal of her uterus). In this situation, doctors often suggest having prophylactic BSO at the same time as the hysterectomy. Still, prophylactic BSO may not make sense for all women at average risk because the decrease in breast and ovarian cancer risk is likely outweighed by the possible long-term risks of prophylactic BSO. Removing the ovaries causes an abrupt drop in estrogen levels; this estrogen drop can harm future bone and cardiovascular health, especially in younger, premenopausal women. Some research suggests that having prophylactic BSO also could cause thinking or memory problems later in life.If you have an abnormal BRCA1 or BRCA2 gene and/or a strong family history of ovarian or breast cancer and haven't had prophylactic BSO, you may want to talk to your doctor about these new guidelines. If you're done having children, prophylactic BSO might make sense for you. Ask your doctor about all of your options to reduce the risk of both ovarian and breast cancer.If you're a breast cancer survivor, you probably should talk to your doctor about prophylactic BSO, no matter your genetic status or family history. Prophylactic BSO can reduce your risk of: the breast cancer coming back developing a new, second breast cancer ovarian cancer You can learn more about prophylactic BSO by visiting the Breastcancer.org Prophylactic Ovary Removal pages.Editor's Note: This article was updated on Jan. 22, 2019, with updated information on cancer risks associated with BRCA mutations. Was this article helpful? Yes / No Was this article helpful? Are these recommendations helpful? Take a quick survey Sign up for emails about breast cancer news, virtual events, and more.Subscribe to our podcast for conversations on the issues that matter most.Join our online community to connect, share, and find peer support. Objective. To establish short-term surgical outcomes of three-port laparoscopic risk-reducing salpingo-oophorectomy (RRSO) in women with hereditary breast-ovarian cancer syndrome (HBOC). Methods. The medical records of all HBOC women that underwent laparoscopic RRSO between January 2001 and December 2010 were retrospectively reviewed. Demographic data, operative details, and short-term surgical outcomes were obtained and subjected to SAS. Statistical univariate and multivariate analyses were performed. Results. 358 patients met study criteria with 277 (77.4%) carrying a documented BRCA mutation. The predominant technique utilized three ports (two 5 mm and one 10/12 mm), a 5 mm laparoscope and a 5 mm Ligasure pulsatile bipolar device. Mean operative time was 58.3 minutes (SD 22.6, 26.0–197.0), significantly affected by BMI greater than 30 ($P < 0 . 0 0 0 1$) and status of adhesions ($P = 0 . 0 0 1$). Estimated blood loss (EBL) was negligible in 96.9% of cases. Seven patients required conversion to laparotomy. No major intraoperative complications were recorded. One-night hospital admission rate was less than 2.0% while postoperative complication rate was 3.1%. Malignancy was revealed in 14 patients (3.9%). Conclusion. In HBOC population, three-port laparoscopic RRSO is a simple, reproducible, and safe procedure with low conversion rate, short operative time, minimal EBL, low surgical morbidity, and rapid postoperative recovery. 1. IntroductionRisk-reducing salpingo-oophorectomy (RRSO) is considered the gold standard for ovarian, fallopian, and primary peritoneal cancer prevention in women with documented BRCA-1 and -2 mutations or family history consistent with hereditary breast-ovarian cancer syndrome (HBOC) [1, 2]. RRSO reduces HBOC women's estimated 10–65% lifetime risk of developing ovarian cancer by approximately 80–96% and their overall mortality by 76% [3–5]. In addition, RRSO has been found to halve the risk of breast cancer in premenopausal HBOC women who have not undergone prophylactic mastectomy [6], while improved quality of life, including satisfaction and mitigation of cancer risk anxiety, has also been reported by women who elected this procedure [7, 8]. However, skepticism regarding RRSO-related surgical risks is frequently encountered during the decision-making process. Despite its common utilization in the general population, short-term surgical outcomes, morbidity, and overall safety of standardized laparoscopic salpingo-oophorectomy (LSO) in the particular cohort of HBOC women have not been established thus far. The application of LSO for risk-reducing purposes is often accompanied by considerable differences compared to reports derived from the general population. This is mostly attributed to the higher rate of previous abdominal surgeries performed in HBOC women, including transverse rectus abdominis myocutaneous (TRAM) flaps for breast reconstruction. Age ≤45 years and absence of hormone replacement therapy at the time of surgery have also been considered risk factors for surgical complications and morbidity associated with RRSO [9]. Furthermore, data derived from HBOC population are limited to a few studies [10–13] with relatively small number of patients, mostly of undefined genetic status, and wide variations in their outcomes. The information gap becomes even more apparent with the emergence of minimally invasive alternatives, such as laparoendoscopic single-site surgery (LESS) [14]. According to preliminary data, LESS represents a feasible technique with excellent clinical outcomes and overall low perioperative complication rates, provided that both laparoscopic surgical expertise and optimal instrumentation are available. However, a thorough short- and long-term assessment in HBOC women, based on comparative baseline data of conventional laparoscopy, is still missing. We undertook a retrospective study evaluating our ten-year experience on standardized approach to laparoscopic RRSO, as utilized in a pure cohort of HBOC women. We aim to establish a reference point in HBOC population for short-term surgical outcomes and overall safety of this procedure, the contemporary information of which can facilitate counseling and decision-making process and can serve as a comparative baseline for developing techniques, such as LESS.2. Material and Methods2.1. Study Population An institutional-review-board- (IRB-) approved retrospective analysis of all women who underwent consented RRSO at Brigham and Women's Hospital between January 2001 and December 2010 was performed. Eligible for inclusion were those women who, regardless of prior surgical history, were referred to our service by the Cancer Risk and Prevention Clinic of Dana-Farber Cancer Institute as meeting the criteria for risk-reducing surgery (Table 1). Women with synchronous abnormalities detected in their preoperative pelvic ultrasound as well as those who underwent RRSO with concomitant hysterectomy and/or other surgical procedures were excluded from the study. Once patients were selected, individual subject data were retrospectively collected from institution's longitudinal medical records (LMRs).Proven germline mutations in BRCA1 or BRCA2 genes in themselves or at least one of their close relatives ORPersonal history of breast cancer before the 36th year of age ORFamily history of breast and/or ovarian cancer even in the absence of an identifiable mutation with(i) at least two first-degree relatives diagnosed with cancer: at least one with invasive breast cancer before the age of 41 years or ovarian cancer at any age OR(ii) three first- or second-degree relatives from the same lineage diagnosed with breast and/or ovarian cancer at any age2.2. Surgical Protocol All operations were performed in the Gynecologic Oncology Division of Brigham and Women's Hospital, and second assist was primarily provided by resident or fellow staff. Robotic-assisted approach was not utilized in this cohort. General endotracheal anesthesia was administered, and the patient was prepped and draped in modified dorsal lithotomy position. A Foley catheter and a Jarcho uterine manipulator were placed. After the appropriate safety pause, the umbilicus was infiltrated with local anesthesia to decrease postoperative pain and everted, and a small incision was made through which a Veress needle (Ethicon Endosurgery, Inc.) was passed. Following insufflation, a 5 mm umbilical, a 5 mm right lower quadrant, and 10/12 mm left lower quadrant port were placed under direct vision. In some cases with suspected peritoneal adhesions, entrance into the abdomen was achieved utilizing direct optical entry with either the Hasson technique with a 10 mm scope (Ethicon Endosurgery, Inc.) or, alternatively, the left upper quadrant approach through Palmer's point with a 5 mm scope. Pelvic washings were obtained and sent for cytological examination. The patient was placed in Trendelenburg position, and after a thorough abdominal and pelvic inspection, the procedure was undertaken with an identical approach in both sides: the ureter was clearly identified; the gonadal pedicle was isolated, clamped, sealed, and divided with ample distance from the ovarian hilum, utilizing a 5 mm LigaSure device (LigaSure, Covidien, Dublin, Ireland); uterine attachments were taken at the cornua, and the ovary was advanced off the pelvic sidewall with care to destroy all the visible proximal fallopian tube; lateral attachments were also sealed; the completely freed ovary and tube were placed into tissue recovery bag and drawn through the 10/12 mm port site for permanent pathologic evaluation. Once hemostasis was ascertained, the lower quadrant ports were removed and the fascial defect from the 10/12 mm port was closed with 0 Vicryl suture. Pneumoperitoneum was released. With all trocars removed, skin incisions were closed with 4-0 Monocryl in a subcuticular fashion. Finally, after the removal of the vaginal instruments and the Foley catheter, the patient was extubated and sent to the day surgical recovery area. Estimated blood loss, presence of adhesions, intra-operative complications, and procedure's length were recorded. All specimens were sent to a dedicated gynecologic pathologist for extensive pathological evaluation including step sectioning of the ovary and distal fallopian tube (SEE-FEM protocol) [15].2.3. Outcome Measures Outcome measures primarily included the safety of RRSO. Conversion rate, duration of hospital stay, and complication rates were used for the assessment of RRSO's safety. Conversion rate was calculated as the proportion of cases that were initiated laparoscopically but converted to laparotomy. Intraoperative complications included vascular or visceral injuries requiring or not blood transfusion. Hospital stay was considered prolonged when medical records indicated hospital admission for one or more nights. All complications during the six-week post-operative followup were recorded with a grade (I, II, IIIa, IIIb, IVa, IVb, or V) assigned according to the modified Clavien-Dindo classification [16]. Specifically, grade I identified the presence of any deviation from the normal postoperative course without the need of intervention or pharmacologic treatment other than antiemetics, antipyretics, analgesics, diuretics, electrolytes, physiotherapy, or wound complications opened at the bedside; grade II identified complications requiring the use of intravenous medications, total parenteral nutrition, enteral nutrition, or blood transfusion; grade III identified complications requiring surgical, endoscopic, or radiologic intervention not under (grade IIIa) or under (grade IIIb) general anesthesia; grade 4 identified life-threatening complications requiring intensive care or intensive care unit management with single (IVa) or multiorgan (IVb) dysfunction; grade 5 identified complications resulting in patient's death. The length of the study period did not allow the utilization of a validated pain-scoring scale. Thus, we evaluated post-operative pain by considering only the cases seeking medical intervention for pain resolution, as recorded in the standard (between 14th and 21st post-operative day) or unscheduled post-operative visits. Cases reporting persistent pain related to the above-mentioned complications were not included. The operative time was assessed from the time of skin incision to the time of skin closure. Estimated intra-operative blood loss was categorized as of less than 50 cc, from 50 to 150 cc and more than 150 cc. Adhesion status was designated as present or absent adhesions without further quantification.2.4. Statistical Analysis We used Fisher's exact tests to compare the characteristics of patients by their genetic status and by type of surgical procedure. Univariate analyses of continuous variables were tested by t-tests and analysis of variance (ANOVA) followed by the Bonferroni post hoc test for all pairwise comparisons. Additionally, we used multivariate linear regression models to examine the mean differences in surgical times by patient characteristics and surgical variables. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).3. Results3.1. Population Characteristics Of all women who underwent risk-reducing surgery at Brigham and Women's Hospital between January 2001 and December 2010, 358 women met our inclusion criteria and were, therefore, subjected to our final analysis. BRCA mutation was identified in 277 patients (77.4%): 147 with BRCA-1 (41.1%), 126 with BRCA-2 (35.2%), and 4 with BRCA-1&2 (1.1%) mutations. Eighty-one patients (22.6%) had a strong family history consistent with HBOC syndrome: 43 were BRCA negative and 38 had not been tested by the end of the study. Mean age at the time of RRSO was 48.1 years (SD 9.2, range 24.0–76.0). As expected, patients with BRCA-1 mutation underwent RRSO at a significantly younger age (45.9 years, SD 8.4, range 34–76) when compared to other subgroups ($P = 0 . 0 0 0 5$). This was also reflected in women's menopausal status by the time of surgery. BRCA-1 carriers were more likely to be premenopausal when compared to other subgroups ($P = 0 . 0 2$). 173 of 357 patients (48.5%) had prior history of abdominal surgery with 126 of them having at least one prior laparotomy. 52.9% of women were treated for previously diagnosed breast cancer. Demographic and clinical characteristics of this cohort are summarized in Table 2. Overall* BRCA-1 BRCA-2 BRCA1/2 HBOC *P* Age *N* (%) 358/358 (100%) 147 (41.1%) 126 (35.2%) 4 (1.1%) 81 (22.6%) ANOVA *P* -value 0.0005Mean age (SD) 48.1 (9.2)45.9 (8.4)49.9 (10.2)42.8 (9.7)49.7 (7.9) BMI *N* (%) 349/349 (100%) 145 (41.5%) 124 (35.5%) 4 (1.1%) 76 (21.8%) ANOVA *P* -value 0.84Mean BMI (SD)26.0 (5.2)26.1 (5.1)26.1 (5.6)25.8 (4.9)25.5 (5.1) Pre-menopausal status *N* (%) 188/356 (52.8%) 92 (62.6%) 59 (46.8%) 1 (25.0%) 36 (45.6%) Fisher's exact *P* -value 0.01 Positive previous surgical history *N* (%) 173/357 (48.5%) 70 (47.6%) 63 (50.4%) 1 (25.0%) 39 (48.2%) Fisher's exact *P* -value 0.83 Previous diagnosis of breast cancer *N* (%) 189/357 (52.9%) 79 (53.7%) 67 (53.6%) 2 (50.0%) 41 (50.6%) Fisher's exact *P* -value 0.96 *Refers to the total number of patients (pts) with nonmissing data for the indicated variable. **All variables as assessed by the time of RRSO.3.2. Surgical Variables and Complications Seven patients (2%), who were operated on during the first five years of the study period, required conversion to laparotomy (Table 3). Five cases were converted secondary to extensive intraperitoneal adhesions attributed to previous surgeries or advanced endometriosis. One case was converted because of difficulty in gaining access to the peritoneal cavity and one case because of identified occult malignancy in frozen section. Patients converted to laparotomy had a two- or threenight hospital admission and uneventful recovery. Case no. Year Reason for conversion Prior surgical history* Adhesion status Oper. time (min) EBL Admitted nights Complication**12001Adhesions−Dense108100 cc2None22001Adhesions+Dense88100 cc2None32001Adhesions+Dense12975 cc2None42002Entrance−None66

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