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**Is BRCA mutation screening a cost-effective strategy to improve targeted therapy in serous epithelial ovarian cancer?**J. Scalici<sup>1</sup>, J. Straughn<sup>2</sup>, J. Estes<sup>2</sup>, C. Leath<sup>2</sup>, M. Finan<sup>1</sup>, R. Rocconi<sup>1</sup>.<sup>1</sup>University of South Alabama-Mitchell Cancer Institute, Mobile, AL,<sup>2</sup>University of Alabama at Birmingham, Birmingham, AL.

**Objective:** Germ-line *BRCA* mutation testing is recommended for all patients with serous epithelial ovarian cancer (EOC). Screening may identify patients who would benefit from targeted therapy such as poly adenosine diphosphate ribose polymerase (PARP) inhibitors. The aim of this study was to analyze the cost-effectiveness of *BRCA* screening as a triage tool for targeted therapy.

**Methods:** A decision analysis model evaluated 4 strategies to screen serous EOC patients for germ-line *BRCA* mutations: 1) SCREEN ALL - patients underwent full-length *BRCA* analysis; 2) HIGH-RISK SCREENING - full sequencing was performed on patients who met criteria by personal or family history; 3) NO SCREENING - no patients were tested; 4) ALTERNATE SCREENING - patients were screened by a validated massively parallel sequencing approach to detect 16 genes implicated in hereditary ovarian cancer. Clinical estimates and testing probabilities were calculated from published literature. Costs were estimated from published literature and Medicare reimbursement rates. All patients testing positive for a germ-line mutation received chemotherapy plus targeted therapy. Sensitivity analyses were performed.

**Results:** Using a cohort of 16,000 serous EOC patients, the most cost-effective strategy was NO SCREENING, with a total cost of \$563.2 million (M) and an overall survival (OS) of 56 months. Although HIGH-RISK SCREENING and SCREEN ALL were more effective (OS of 57 months), they had higher total costs. The incremental cost-effectiveness ratio (ICER) for both strategies was unacceptably high at \$14.6 M and \$9.8 M per life-year saved, respectively. While the most effective strategy was ALTERNATE SCREENING with an OS of 59 months and total cost of \$942.7 M, the ICER was \$6.0 M per life-year saved. ALTERNATE SCREENING identified the most mutation-positive patients, but incurred the highest cost due more patients receiving targeted therapy. As the cost of targeted therapy decreased from \$96,750 to \$24,000, ALTERNATE SCREENING dominated TEST ALL and HIGH-RISK SCREENING, making it the only acceptable alternative to NO SCREENING.

**Conclusions:** Currently, it is not cost-effective to offer *BRCA* mutation screening to serous EOC patients to direct therapy. Advances in genomic technology should accelerate the discovery of cancer susceptibility genes and increase the feasibility of evaluating multiple genes simultaneously at lower cost. It is imperative that the cost of targeted therapy be considered relative to its clinical benefit because improved recognition of inherited risk should identify more individuals who are candidates for treatment.

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**Frequencies of nonovarian cancers within the Gilda Radner Familial Ovarian Cancer Registry**

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**Objective:** To determine if the frequency of nonovarian cancers (NOC) within families in the Gilda Radner Familial Ovarian Cancer Registry (GRFOCR) is significantly different from the frequencies listed in the SEER database.

**Methods:** The GRFOCR is a familial ovarian cancer registry established in 1981. The families within this national database are

those with 2 or more close relatives who have a diagnosis of ovarian cancer, 3 or more cases of cancer on one side of the family with at least 1 being ovarian, at least 1 female with 2 or more primary cancers in which one is ovary, or a history of 2 or more cancers in the family with at least one being ovarian cancer diagnosed before the age of 45 years. These data were analyzed using Statistical Analysis System (SAS) to find relative rates of 10 of the most common cancers found within the database, with the exception of ovarian and breast. These include bladder, central nervous system, cervical, colorectal, liver, lung, pancreas, prostate, stomach, and uterine. These data were used to compare frequencies of the cancers within the database with that listed in the SEER 18 database. The data were further adjusted into age-specific frequencies of each cancer, as seen in the SEER database.

**Results:** There are 2,693 pedigrees and a total of 50,277 individuals within the GRFOCR. There are 2011 families with 2 or more relatives with ovarian cancer, accounting for 4,989 individuals with ovarian cancer. The total number of individuals with ovarian cancer is 5,613. The frequencies of the NOCs within the registry were higher than that of the general population, as described in the SEER database. In particular, the overall frequencies of cancers of the bladder, cervix, prostate, and uterus were higher within the GRFOCR at 2.3, 7.4, 25.2, and 11.9 per 1,000, respectively, vs. 1.8, 1.6, 16.4, and 3.8 within SEER. Furthermore, the data show that both cervical and uterine cancers occurred in a higher proportion at an earlier age within the GRFOCR (Table). Compared with the age-adjusted frequencies in the SEER database, our frequencies were statistically significant with a *P* value of <0.01 for all values.

**Conclusions:** The GRFOCR is a powerful, versatile platform that has proven useful for studying not only ovarian, but NOC. To further validate our findings, we will enhance our collection of information on NOC within the GRFOCR. Additional future steps will include conducting segregation analysis as well as genome-wide linkage studies on families with NOC.

**Table. Frequencies of Nonovarian Cancers.**

	≤19 Years	20-34 Years	35-44 Years	45-54 Years	55-64 Years	65-74 Years	>75 Years	n =
<u>GRFOCR</u>								
Bladder	2.6	1.7	6	9.5	13	15.6	51.3	115
Cervical	1.5	31.4	12.5	8.9	4.1	6.2	35	191
Prostate	0	0	0.34	2.7	10.8	20.6	65.3	580
Uterine	0.65	7.1	9.7	17.5	9.7	7.4	47.7	308
<u>SEER</u>								
Bladder	0.1	0.4	1.6	7.4	18.4	27.4	44.7	83,931
Cervical	0.2	14	25.9	23.8	16.7	10.7	8.7	17,257

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**Novel Surgical Techniques**

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**Comparison of aortic nodes yields and metastasis rates above and below the inferior mesenteric artery in clinically low stage carcinomas**K. O'Hanlan<sup>1</sup>, J. Ferry<sup>1</sup>, M. Chivukula<sup>2</sup>, M. O'Holleran<sup>3</sup>. <sup>1</sup>Laparoscopic Institute for Gynecologic Oncology, Portola Valley, CA, <sup>2</sup>Magee-Women's Hospital of UPMC, Pittsburgh, PA, <sup>3</sup>General Surgery Associates, San Carlos, CA.

**Objective:** Compare aortic lymph node metastasis identified above and below the inferior mesenteric artery when aortic lymphadenectomy is indicated in clinically early high-risk endometrial cancer, epithelial ovarian cancer, and fallopian tube carcinoma.

**Methods:** Included were 95 women with clinical stage I and II uterine, 34 with IB cervical carcinoma, and 34 with tubal/ovarian cancer with no gross metastatic lesions. One hundred sixty-three had bilateral pelvic lymphadenectomy, 82 had bilateral inframesenteric (IM) aortic lymphadenectomy, and 71 had bilateral infrarenal (IR) lymphadenectomy. All underwent LH, bilateral salpingo-oophorectomy, appendectomy, and peritoneal washings for cytology with or without infracolic omentectomy. Statistical analysis was performed using independent t-test and ANOVA for comparison of means and chi-square for categorical variables.

**Results:** The mean age was 56 years (range, 27–90 years), mean body mass index was 28.3 (range, 17.2–50). The median number of pelvic, IM, and IR nodes harvested was 24 (range, 1–32), 11 (range, 1–26), and 14 (range, 1–28), respectively. There was no difference in procedures or nodal yields between the 3 primaries, so all were considered together. Lymph node metastasis was found in 34 (21%) patients: 29/163 (18%) pelvic, 18/82 (22%) IM, and 13/71 (18%) IR. Among the 29 with positive pelvic nodes, 15 (52%) had positive aortic nodes, 13 (45%) had positive IM nodes, and 11 (38%) had positive IR nodes. Among the 134 with negative pelvic nodes, 5 (4%) had positive aortic nodes, 4 (5%) had positive IM nodes, and 2 (1.5%) had positive IR nodes. Among the 17 with positive IM nodes, 13 (76%) had positive pelvic nodes and 10 (59%) had positive IR nodes. Among the 13 with positive IR nodes, only 2 had negative IM nodes, and 2 had negative pelvic nodes. Ten of 13 with positive IR nodes had high-grade endometrial carcinoma. The rate of nodal metastasis increased significantly with the number of nodes harvested (95% CI 0.093–0.26,  $P < 0.0001$ ). A total of 7/34 (21%) of stage IB cervical cancer patients, 23/95 (24%) stage I or II endometrial cancer patients, and 4/34 (12%) patients with ovarian/tubal carcinoma were upstaged from lymphadenectomy alone.

**Conclusions:** Comprehensive laparoscopic lymphadenectomy for early pelvic carcinomas is feasible, with acceptable nodal yields. Nodal metastasis was identified up to the renal vessels in 18% of cases, most often when the pelvic and inframesenteric nodes were involved. Obtaining more nodes resulted in higher rates of upstaging and more appropriately aggressive therapy.

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### Impact of obesity on surgical outcomes of laparoscopic radical pelvic lymphadenectomy for women with cervical, endometrial, or ovarian cancer

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**Objective:** Gynecologic oncologists performing traditional laparotomy for staging hysterectomy with radical pelvic lymphadenectomy who desire to transition to minimally invasive approaches may be deterred by the increasing rates of obesity in women today. We document the impact of obesity on surgical adequacy and complication rates from a minimally invasive approach to laparoscopic radical pelvic lymphadenectomy across the body mass index (BMI) spectrum.

**Methods:** Institutional review board approval was maintained at the primary hospital. Data were abstracted from medical records for all patients undergoing a laparoscopic radical pelvic lymphadenectomies

for cervical, endometrial, tubal, or ovarian carcinoma from 9/1/1996 to 7/26/2012. Statistical analysis was performed using independent t-test and ANOVA for comparison of means and chi square for categorical variables.

**Results:** A total of 159 women underwent laparoscopic radical pelvic lymphadenectomy. The mean age was 54 years (range, 27–90 years), weight was 74 kg (range, 43–135 kg), and BMI was 28.5 (range, 17.8–50.3). At final pathology, 92 (58%) had endometrial carcinoma/sarcoma, 34 (21%) had cervical carcinoma, 30 (19%) had ovarian/tubal carcinoma, and 3 (1.9%) had endometrial and ovarian primaries. Women were stratified by obesity: 107(67%) had BMI < 29.9, 45(28%) had BMI 30–39.9, and 7(4%) had BMI > 40. Complications occurred in 13 (8%) patients; 7 were reoperative, including 1 each pelvic abscess, vaginal cuff bleed, ureteral stenosis, bowel obstruction, and cystotomy repair and 2 incisional hernias. Six complications were not reoperative, with 1 each subcutaneous hematoma, colotomy repair, and cystotomy repair, and 3 with pelvic cellulitis, not related to BMI (NS). The mean surgical duration for ideal/overweight was 202 minutes (NS). The mean blood loss was: 183 mL for ideal/overweight, 129 mL for obese, and 314 mL for morbidly obese ( $P < 0.0104$ ). Three patients required transfusion, unrelated to BMI (NS). The mean hospital stay for all BMI categories was 1.4 days (NS). The mean pelvic node yield was 23 (NS). Pelvic nodes were positive in 22/107 (21%) of ideal/overweight, 6/45 (13%) of obese, and 0/7 (0%) of morbidly obese ( $P < 0.0001$ ). Notably, the chance of finding positive nodes increased significantly with increasing number of pelvic nodes harvested ( $P = 0.0001$ ).

**Conclusions:** Surgeons can expect to successfully perform radical pelvic lymphadenectomy across the BMI spectrum with low complication and transfusion rates. These data affirm existing data suggesting that complete lymphadenectomy more accurately reveals nodal positivity.

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### Transperitoneal versus retroperitoneal approach for staging aortic lymph- adenectomy

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**Objective:** Assess safety and feasibility of transperitoneal and retroperitoneal aortic lymphadenectomy up to the renal veins in early endometrial, tubal, and ovarian cancer patients.

**Methods:** A retrospective chart review was undertaken. Statistical analysis was performed using independent t-test and ANOVA for comparison of means and chi square for categorical variables.

**Results:** Seventy-two patients underwent laparoscopic hysterectomy with comprehensive staging from 12/1996 to 8/2012. A total of 30 (42%) aortic lymphadenectomies were performed by initial transperitoneal approach, and 42 (58%) were performed by retroperitoneal approach. Omentectomy was performed in 36/72 patients, with no difference between groups. Two (4%) of the retroperitoneal approaches were converted to open procedures due to a transection of the renal artery in one patient and bleeding with loss of pneumoretroperitoneum in another. All transperitoneal approach dissections were successful. Nonreoperative complications included 1 ureteral kinking requiring stenting, 1 vaginal cuff bleed, and 1 pelvic cellulitis. Total surgical duration (includes total laparoscopic hysterectomy/bilateral salpingo-oophorectomy/appendectomy/pelvic lymphadenectomy) for the both groups was 227 minutes (NS). Mean estimated blood loss totals for the entire procedure (including hysterectomy on all) for the transperitoneal and retroperitoneal