A Cost Analysis of Colposcopy following Abnormal Cytology in Post-treatment Surveillance for Cervical Cancer

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Objective: To determine the cost and outcomes associated with performance of colposcopy and biopsies following an abnormal Pap test (Pap) for women with a history of invasive cervical cancer.

Methods: Simple decision models were constructed to compare the costs and the number of isolated local recurrences detected using two strategies for women with a history of cervical cancer and an LSIL/ASCUS+HPV (low grade) or an HSIL (high grade) Pap: (1) colposcopy or (2) no colposcopy. Outcomes were modeled based on cohorts of 50 women with a low grade Pap and 78 women with a high grade Pap following a diagnosis of invasive cervical cancer. Costs of colposcopy and of treatment for high grade dysplasia were obtained using national reimbursement data.

Results: We identified 556 patients with invasive cervical cancer who met inclusion criteria and collectively underwent 2,900 surveillance Paps. Of the 97 patients in the cohort who were diagnosed with a recurrence, 28.9% had either a low grade or high grade surveillance Pap result. Among 50 women with a low grade Pap, 27 underwent colposcopy and 23 did not. Of the 3 recurrences in the colposcopy group, only one was an isolated local recurrence and was diagnosed with colposcopy. Of the 6 recurrences in the no colposcopy group, two were isolated local recurrences and both were diagnosed with non-colposcopic diagnostic methods. For low grade Pap, the colposcopy strategy cost on average $354 more than no colposcopy and resulted in a lower rate of diagnosis of isolated pelvic recurrence compared to non-colposcopy diagnostic methods (3.7% vs 8.6%). Among 78 women with a high grade Pap, 60 underwent colposcopy and 18 did not. Of the 15 recurrences in the colposcopy group, five were isolated local recurrences diagnosed with colposcopy. Of 4 recurrences in the no colposcopy group, none were isolated local recurrences. For high grade Pap, colposcopy cost on average $623 more than the no colposcopy strategy, but resulted in a higher rate of diagnosis of isolated local recurrence than the no colposcopy strategy (8.3% versus 0%). Colposcopy following high grade Pap was associated with a cost of $7481 per additional isolated local recurrence detected.

Conclusions: Colposcopy following low grade Pap adds significant cost and does not appear to increase the probability that cervical cancer recurrence will be detected when salvageable. Colposcopy following a high grade Pap also adds significant cost, but appears to be associated with a higher probability that cervical cancer recurrence will be detected when salvageable. These findings support withholding colposcopy for abnormal Pap tests less than high grade in this population.
Bevacizumab beyond progression is not associated with prolonged progression-free survival in epithelial ovarian cancer

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Objective: To evaluate the efficacy and safety of bevacizumab beyond progression (BBP) in patients with epithelial ovarian cancer (EOC).

Methods: A multicenter retrospective analysis of patients with EOC who received bevacizumab was conducted. Patients who were treated with front-line bevacizumab and recurred were separated based on whether they received any treatment with BBP: (1) No further bevacizumab (2) BBP at first or second recurrence (BBP1/2); or (3) BBP at third or fourth recurrence (BBP3/4). Another group consisted of those who did not receive front-line bevacizumab, but were treated with bevacizumab at first recurrence.

Progression-free (PFS) and overall survival (OS) were analyzed using the Kaplan-Meier method and compared between groups using the log-rank test.

Results: 385 eligible patients were identified. 81 patients received front-line bevacizumab, subsequently recurred, and received either (1) no BBP treatment (69%; n=56); (2) BBP1/2 (22%; n=18); or (3) BBP3/4 (9%; n=7). 65 patients did not receive bevacizumab until first recurrence. There was no difference in OS between the treatment groups. However, PFS was statistically superior in the group that did not receive BBP compared to those treated with BBP1/2 (11 vs. 7 months; \(p=0.04\)); or BBP1-4 (11 vs. 8 months; \(p=0.01\)); or those who did not receive bevacizumab until first recurrence (11 vs. 5 months; \(p=0.01\)).

Conclusions: These findings do not suggest that continued VEGF inhibition with bevacizumab beyond progressive disease is useful in the management of previously bevacizumab-treated patients with EOC. However, there may be a PFS benefit toward using bevacizumab front-line rather than reserving this therapy for first recurrence.
Ovarian Carcinosarcoma: Effects of Cytoreductive Status and Platinum-Based Chemotherapy on Survival

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Objectives: Ovarian carcinosarcoma (OCS) is a rare and aggressive pathology. The study purpose was to define survival patterns of OCS based on patient and tumor characteristics, cytoreduction and adjuvant therapy.

Methods: A single institution, retrospective chart review and social security death index search were performed on women diagnosed with OCS from 2/1993 to 5/2009. Comparisons were made with the Wilcoxon’s rank sum tests, chi-square, or Fisher’s exact tests. Risk of death was characterized by univariate and Cox proportional hazards model. Kaplan-Meier Survival Curves were constructed.

Results: Forty-seven cases of primary ovarian carcinosarcoma were identified. Median age was 66 and median follow-up and survival was 25.8 months. Seventy-five percent had advanced disease at diagnosis. The median preoperative CA-125 was 117 U/mL. Optimal cytoreduction was possible in 70.2% of cases; 51.1% were left with no residual disease. Lymphadenectomy (LAD) was performed on 27.7%, and CA-125 levels and performance of lymphadenectomy were not significantly associated with survival. Age conveyed a risk for death with a Cox proportional HR 3.28 (95% CI 1.51-7.11, p =0.003). Compared to stages I and II, Stage III carried a HR for death of 4.75 (95% CI 1.16-19.4, p = 0.03) and stage IV disease carried a HR of 9.13 (95% CI 1.76-47.45, p = 0.009). Those with >1 cm of residual disease had a HR for death of 4.71 (95% CI 1.84-12.09, p = 0.001) compared to those cytoreduced to no gross residual disease. This remained significant when only looking at stage III and IV disease with a HR for death of 3.41 (95% CI 1.21-9.62) for those with >1 cm residual disease compared to those cytoreduced to no residual disease. Postoperatively, 22 (57.9%) received platinum-based chemotherapy, while 13 (34.2%) received a non-platinum based chemotherapy regimen. Three (7.9%) received radiation therapy alone. At analysis, 59.1% of those who received platinum-based chemotherapy were alive, compared to 23.1% of those who received non-platinum based chemotherapy (p=0.08).

Conclusions: Ovarian carcinosarcoma is often advanced stage at diagnosis and behaves aggressively. Age, stage, and cytoreduction to no gross residual disease are associated with improved survival. Cytoreduction to no residual disease should be the goal of surgical management. Platinum-based chemotherapy may be preferable to other regimens, but the ideal adjuvant treatment regimen has yet to be determined.
Incidence of occult micrometastases in superficial inguinal lymphadenectomy specimens in patients with recurrent vulvar cancer.

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**Objective:** To determine the frequency of micrometastases in recurrent early stage vulvar cancer patients with negative lymphadenectomy specimens by conventional histologic analysis and to evaluate clinicopathologic differences between local and distant recurrences.

**Methods:** The records of patients with a diagnosis of squamous cell vulvar cancer at the University of North Carolina from 1993 to 2010 were reviewed. Eighty-five patients were identified that underwent a primary complete resection and a negative inguinal lymph node dissection as initial treatment. Demographics and pathology data for patients with local and distant recurrences was extracted. Twenty-five patients (29.4%) with a histologically negative lymph node dissection developed a recurrence. All available lymph node tissue was serially sectioned and ultrastaged with H&E staining and with pancytokeratin antibody (AE1/AE3) immunohistochemical (IHC) staining to detect micrometastasis. 5 patients were excluded secondary to incomplete pathologic material for evaluation.

**Results:** In our study cohort of 20 patients, the median age at diagnosis was 64.5 years (range 32 to 84). Five (25%) patients had a unilateral lymphadenectomy, and 15 (75%) patients had a bilateral lymphadenectomy. Seventeen (85%) patients had stage IB disease, and 3 (15%) patients had stage II disease. The median progression free survival was 25.8 months (range 5.8-112). Local recurrence (LR) occurred in 14 (70%) patients while 6 (30%) patients recurred in the groin and/or at distant sites (GDR). No micrometastases were detected in the lymph nodes of any LR patient; a micrometastasis was found in only 1 (16.6%) GDR patient. Univariate comparison of clinicopathologic factors in the LR and GDR cohorts revealed significantly older patients in the LR group (median age 72 vs. 48, p< 0.002) and more frequent moderately or poorly differentiated lesions in the GDR group (83.3% vs. 50%, p=0.016). Tumor size, depth of invasion, presence of lymphovascular space invasion, closest margin, number of lymph nodes/groin, and BMI were not associated with LR or GDR.

**Conclusions:** The addition of serial sectioning and ultrastaging with H&E and AE1/AE3 IHC staining in the pathologic evaluation of inguinal lymph nodes does not increase the detection of lymph node metastasis in patients with primary squamous cell carcinoma of the vulva and did not correlate with GDR. The low incidence of micrometastasis may further support the role of sentinel lymph node dissection in the management of patients with vulvar cancer. Younger age and increasing grade were associated with GDR in our patient population.
The Effect of Lower Uterine Segment Involvement in the Recurrence Patterns of High Grade Endometrial Cancer

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**Objectives:** Patterns of recurrence are crucial to decision making for adjuvant treatment recommendations. We sought to characterize patterns of recurrence amongst high-grade endometrial cancers.

**Methods:** A retrospective review of all endometrial cancer cases from 2005 to 2010 was performed. Cases with high grade histology and pathologic documentation of lower uterine segment (LUS) involvement were included. Descriptive analyses were performed using frequencies. Bivariate statistical analysis was performed using Chi square and multivariate regressions were performed by logistic regression modeling.

**Results:** 329 cases met inclusion criteria. 171 cases were LUS+ (52%) and 158 were LUS- (48%). Within the LUS+ group, 132 (80.0%) had adjuvant therapy as compared to 97 (63.4%) in the LUS- group (p=0.001). In the LUS+ group, there were 73 recurrences (42.7%) compared to 36 recurrences (22.8%) in the LUS- group (p<0.000).

The women with LUS+ tumors were divided into four groups based on type of adjuvant therapy: 1) 35 patients received only chemotherapy (CT) with 25 recurrences (71.4%), 2) 24 patients had radiation (RT) only with 7 recurrences (29.2%), 3) 70 patients had CT and RT with 31 recurrences (44.3%), and 4) 39 patients had no adjuvant therapy with 10 recurrences (25.6%). Those without LUS involvement were similarly analyzed: 1) 23 patients received only CT with 12 recurrences (52.2%), 2) 23 patients had RT only with 4 recurrences (29.2%), 3) 49 patients had CT and RT with 7 recurrences (14.3%), and 4) 61 patients had no adjuvant therapy with 12 recurrences (19.7%).

Evaluation of the recurrence locations in women with LUS+ tumors showed 20.0% vaginal, 17.1% pelvic, and 62.86% abdominal and distant recurrences. The LUS-tumors were distributed with 19.2% at the vaginal cuff, 8.2% in the pelvis, and 72.6% in the abdomen or more distant. There was no significant difference in recurrence pattern between LUS+ and LUS- tumors, even when controlling for adjuvant treatment, stage, LVSI, and myometrial invasion. Only tumor stage had a significant effect on recurrence location, with higher stage being associated with increased incidence of abdominal recurrence (p=0.004).

**Conclusions:** Lower uterine segment involvement was associated with a higher recurrence rate despite a greater percentage of patients in this group receiving adjuvant therapy. This suggests that lower uterine segment involvement should be taken into account when assessing a women’s recurrence risk from endometrial cancer. In addition, improvements need to be made in adjuvant therapy for these women with LUS+ endometrial tumors, given their high risk of recurrence with our current treatment strategies.
The COX-2 inhibitor, celecoxib, exhibits anti-tumorigenic and anti-metastatic effects for ovarian cancer in vitro and in vivo.

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Objectives: COX-2 inhibitors have demonstrated promise in the treatment and prevention of many malignancies, based on in vitro, in vivo and epidemiological studies. COX-2 overexpression has been linked to worse outcomes and platinum resistance in ovarian cancer. Thus, our overall goal was to evaluate the effect of COX-2 inhibitors on (1) proliferation, apoptosis and telomerase activity in human ovarian cancer cell lines, and (2) inhibition of tumor growth in a genetically engineered mouse model of ovarian cancer.

Methods: Three ovarian cancer cell lines, SKOV3, HEY, and IGROV1, were used in these studies. Cell proliferation was assessed by MTT assay after exposure to the COX-2 inhibitor, celecoxib. Cell cycle progression was evaluated by flow cytometry. Apoptosis was assessed by ELISA for caspase-3. hTERT mRNA expression was assessed by real-time RT-PCR. Western immunoblotting was performed to determine the effect of celecoxib on COX-2 expression in the ovarian cancer cell lines. Adhesion was assessed by ELISA assay and invasion was assessed by ChemoTx assay. The K18-gT121+/−;p53−/−;Brcal−/− (KpB) mice were subjected to a 60% calories-derived from fat in a high fat diet (HFD) versus 10% calories from fat in a low fat diet (LFD) to mimic diet-induced obesity and subsequently exposed to celecoxib or placebo for 4 weeks.

Results: Celecoxib significantly inhibited proliferation in a dose-dependent manner in all three ovarian cancer cell lines (IC₅₀ 25 μM for SKOV3, 25 μM for HEY and 50 μM for IGROV1) (p=0.0001-0.0002) after 48 hours of exposure. Treatment with celecoxib resulted in G1 cell cycle arrest and induction of apoptosis. In addition, celecoxib inhibited hTERT mRNA expression in all three cell lines. Western immunoblot analysis demonstrated that celecoxib treatment suppressed COX-2 expression within 24 hours of exposure. Cellular adhesion was decreased by 20-40% in all cell lines at a dose of 25 mM (p=0.002-0.009) and at 50 mM (p=0.00001-0.02). In addition, cellular invasion was decreased in all cell lines in a dose dependant manner (p<0.001). In the KpB mice fed a high fat diet and treated with celecoxib, tumor weight decreased by 70% (p=0.04) when compared with control animals. Among KpB mice fed a low fat diet, tumor weight decreased by 25% after treatment with celecoxib, but this was not statistically significant.

Conclusion: Celecoxib potently inhibited cell growth via G1 arrest, decreased telomerase activity, increased apoptotic cell death, and decreased cellular adhesion and invasion in human ovarian cancer cells. In vivo studies using the KpB mouse model found that treatment with celecoxib was more efficacious in inhibiting tumor growth among mice fed a high fat diet. Obesity, insulin resistance and inflammation are tightly linked with cancer development and progression, and this may explain the preferential effect of celecoxib in the obese KpB mice. This work suggests that celecoxib may be a novel chemotherapeutic agent for ovarian cancer prevention and treatment that is potentially more beneficial in the obese population.
The effects of NT1014, a novel AMPK activator, on cell proliferation and apoptosis.

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Objectives: Anti-diabetic biguanide drugs, such as metformin, have been shown to have anti-tumorigenic effects by behaving as AMPK activators and mTOR inhibitors. NT1014 (NovaTarg Therapeutics) is a novel AMPK activator that enters cells specifically through the organic cation transporter, OCT1. Thus, we sought to assess the effect of NT1014 on cell proliferation and apoptosis in human ovarian cancer cell lines.

Methods: Ovarian cancer cell proliferation was assessed by MTT assay after exposure to NT1014. Apoptosis was analyzed by Annexin V-FITC assay. Cell cycle progression was evaluated by flow cytometry. Phosphorylated-S6, phosphorylated-AMPK, pan-S6, pan-AMPK and OCT1 were evaluated by Western immunoblotting analysis.

Results: NT1014 significantly inhibited proliferation in a dose-dependent manner in both ovarian cancer cell lines (IC50 1000 μM for SKOV3, 500 μM for IGROV1), within 48 hours of exposure. Treatment with NT1014 resulted in G1 cell cycle arrest in both cell lines. Apoptosis occurred in IGROV1 cells exposed to NT1014, but not in SKOV3 cells. Western immunoblot analysis demonstrated that NT1014 induced phosphorylation of AMPK, its immediate downstream mediator, within 48 hours of exposure. In parallel, treatment with NT1014 decreased phosphorylation of the S6 protein, a key downstream target of the mTOR pathway. Expression of OCT1 was also decreased in a dose-dependent fashion.

Conclusion: NT1014 inhibited ovarian cancer cell growth, predominantly through G1 cell cycle arrest. More work is needed to determine if metformin and its novel agents, such as NT1014, will be beneficial in the treatment of women with ovarian cancer.
Phenformin Suppresses Proliferation and Induces Apoptosis in Endometrial Cancer Cell Lines.

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Objectives: Obesity and diabetes have been linked to worse outcomes in women with endometrial cancer. Metformin is a biguanide drug that is widely used for the treatment of type II diabetes and has been found to have anti-tumorigenic effects via AMPK activation and inhibition of the mTOR pathway. Phenformin is another biguanide with anti-diabetic activity that was withdrawn from the market due to a small risk of lactic acidosis (64 cases per 100,000 patient-years), higher than that seen with metformin. Studies in breast cancer animal models suggest that phenformin may be more potent for inhibiting tumor growth than metformin. Thus, our goal was to assess the effect of phenformin on proliferation and apoptosis in endometrial cancer cell lines.

Methods: Two endometrial cancer cell lines (ECC-1 and Ishikawa) were used in these studies. Cell proliferation was assessed by MTT assay after exposure to phenformin. Cell cycle progression was evaluated by Cellometer. Apoptosis was assessed by Annexin V-FITC assay. Phosphorylated-AMPK, pan-AMPK, phosphorylated-S6, and pan-S6 were assessed by western immunoblot in the endometrial cancer cell lines.

Results: Phenformin significantly inhibited proliferation in a dose-dependent manner in both endometrial cancer cell lines (IC50 for both ECC-1 and Ishikawa was 1 mM at 40 hours) (p = 0.02 - 0.0004 for ECC-1; p = 0.011 - 0.0002 for Ishikawa). Treatment with phenformin resulted in G1 cell cycle arrest and induction of apoptosis. Western immunoblot analysis demonstrated that phenformin induced phosphorylation of AMPK, its immediate downstream mediator, within 18 hours of exposure. In parallel, treatment with phenformin decreased phosphorylation of S6 protein, a key target of the mTOR pathway.

Conclusion: Phenformin potently inhibited endometrial cancer cell growth via G1 arrest and increased apoptosis. Although the risk/benefit ratio clearly favors metformin over phenformin for the treatment of diabetes, this may not hold true for the treatment of cancer if phenformin was found to have superior anti-tumorigenic activity. More work needs to be done to explore the benefits of both metformin and phenformin for the treatment of endometrial cancer, a disease strongly associated with obesity and diabetes.
A Multimodal Pain Management Protocol for Gynecologic Oncology Surgery

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Objective: To determine if the institution of a multimodal pre and postoperative pain management protocol that includes the use of pregabalin, celecoxib and acetaminophen in addition to continuous local anesthetic wound infusion leads to reductions in postoperative opioid use, improved patient pain assessment ratings, and decreased postoperative complications commonly related to opioid use in patients undergoing gynecologic oncology surgery.

Methods: We conducted an IRB approved retrospective cohort study of patients, who underwent open surgery by Gynecologic Oncology surgeons at Thomas Jefferson University Hospital from August 2011 to July of 2012. In January 2012 the division of Gynecologic Oncology instituted a multimodal pain management approach that added preoperative administration of pregabalin, celecoxib, and acetaminophen, with postoperative continuation of the latter two medications, to the standard pain management approach (three days of continuous subfascial local anesthetic wound infusion, NSAIDs, ibuprofen or ketorolac and opioids). Patients who received the multimodal protocol were compared to a control cohort identified from all patients in the 5 months prior to the transition in standard of care. The primary outcome of the study was postoperative opioid use measured in morphine equivalents. Secondary outcomes included changes in patient pain assessment ratings and side effects commonly associated with opioid use. All statistical analyses were performed using SPSS 20.0 with a p-value of <0.05 considered statistically significant.

Results: We identified a total of 52 patients who met inclusion criteria – 26 control patients who received the standard pain management protocol and 26 study patients who received the multimodal pain protocol. Patients who received the multimodal pain protocol used significantly lower amounts of total opioids (43.3 ± 36.7 v 86.3 ± 41.1 in the control group p=0.001) and used significantly fewer doses of anti-emetics (1.2 ± 1.2 v 1.7 ± 2.3 p=0.04). Pain assessment rating scores were not significantly different between the two groups, however, except for post-operative day 4, these scores were lower in the study cohort. There were no significant differences in the incidence of postoperative complications including ileus, small bowel obstruction, transfusion, wound toxicity, pneumonia or fever.

Conclusion: A pre and post operative multimodal pain management approach that includes pregabalin, celecoxib and acetaminophen in addition to subfascial local anesthetic wound infusion and the traditional use of opioids results in a significant decrease in postoperative opioid and antiemetic use as well as a general trend toward lower patient reported pain assessments.
Objective: To identify the physical factors influencing the risk of slipping when patients are placed in Trendelenburg for minimally invasive gynecologic surgery.

Methods: IRB exclusion was granted. A mannequin, similar to an average female patient, functioned as a human surrogate. The mannequin was placed in the dorsal supine position on an operating table and amount of Trendelenburg was increased until the mannequin slipped. The angle of the bed when slipping was first observed (slip angle) was measured using a Swanson angle finder and repeated in triplicate. The influence of the following variables: mannequin weight (100-250 lbs. in 50 lbs. increments), bed surface (a standard bed sheet, egg crate foam, and a gelpad), and operating room table model (Steris AMSCO 3085 SP and Skytron 6701 Hercules), were evaluated. An ANOVA with a Tukey post-hoc analysis was used to compare means, p<0.05 was deemed significant.

Results: The weight of the mannequin did not significantly affect the slip angle on the egg crate foam or gelpad surfaces. However, on the bed sheet alone, the slip angle was significantly greater at the 250 lbs. than at all other mannequin weights tested (250 vs. 100 lbs. p=.007, 150 lbs. p=.001, or 200 lbs. p=.005). The bed surface had no significant effect on the slip angle for the 100, 150, and 200 pound tests; but at 250 lbs., the mannequin’s slip angle was only significantly increased on the bed sheet compared to the gelpad (28.7˚ vs. 23.7˚ p=.020). The mannequin had a greater slip angle on the Skytron versus the Steris operating room table at the 100 (23˚ vs. 14˚ p=.002), 200 (23˚ vs. 18˚ p=.006), and 250 (29˚ vs. 21˚ p=.001) pound test weights on the bed sheet surface.

Conclusions: Lighter patients were found to be more prone to slipping in our model but this was only found in the patients on the bed sheet. Operating room table choice can mitigate the risk of slipping.
Long-term Recurrence Rates After Robot-assisted Surgical Treatment of Early Cervical Cancer: A Single Institution’s Experience

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Objectives: Previous studies have established the feasibility and safety of robotic surgery in early cervical cancer. The goal of our study was to report long-term survival and recurrence-free interval outcomes for patients surgically treated using robotic-assisted laparoscopy.

Methods: This was an IRB approved retrospective chart review for all cervical cancer patients at the University of North Carolina Hospital from 2005 to 2011. Patients with Stage IA1, IA2, IB1, IB2, and IIA cervical cancer that underwent a robotic-assisted laparoscopic surgery including hysterectomy, radical hysterectomy, parametrectomy, and trachelectomy were included. Demographics, pathology data, overall survival, and recurrence-free intervals were analyzed. Statistical analysis using Chi-square, t-test, and Kaplan-Meier curves were performed with STATA software.

Results: A total of 141 patients were identified and included in the study. The surgical treatments included 111 (79.8%) patients underwent a radical hysterectomy, 13 (9.4%) patients underwent a trachelectomy, 9 (6.5%) patients underwent a parametrectomy after hysterectomy, and 6 (4.3%) patients underwent a simple hysterectomy. Ten (7.2%) patients had Stage IA1 disease, 11 (7.9%) patients had Stage IA2, 107 (77.0%) patients had Stage IB1, 9 (6.5%) patients had IB2, and 2 (1.4%) patients had Stage IIA1. The mean age was 44.2 (range 17-75) and the mean body mass index was 27.7 (16-50). The mean follow up time was 24.9 (range 0-82.1). Overall survival was 97.1%. Recurrence was documented in 4 (2.8%) patients.

Conclusion: Based on the longest available follow up for early cervical cancer treated with robotic surgery, robotic-assisted surgery does not adversely affect survival or rates of recurrence. These findings provide further evidence that robotic-assisted laparoscopic surgery staging is not associated with inferior results when compared to laparotomy or traditional laparoscopy.
Influence of obesity on robotic hysterectomy outcomes in the gynecologic oncology population
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Objective: To determine the influence of obesity on robotic hysterectomy outcomes among patients with gynecologic cancer, including short term complications, length of hospital stay (LOS), conversion to laparotomy, length of procedure, estimated blood loss (EBL), and change in hemoglobin.

Methods: Retrospective review of all patients who underwent robotic gynecologic surgery at a single community hospital from the initiation of robotic gynecologic surgery in October 2007 through April 2011. Data collected included patient age, body mass index (BMI), pathologic diagnosis, LOS, American Society of Anesthesiologists (ASA) Physical Status classification system score, length of procedure, conversion to laparotomy, EBL, pre and post-operative hemoglobin. Statistical analysis included the Spearman rank order correlation, Chi-Square test, Mann-Whitney rank sum test, and logistic regression.

Results: A total of 238 patients underwent robotic gynecologic surgery, with 83 (35\%) having a diagnosis of invasive cancer. Among all patients, a diagnosis of malignancy was associated with an increased length of stay (p=0.0041, OR 2.42) and an 8-fold increased risk of conversion to laparotomy. In addition, there was a trend toward increased risk of short-term complication (13.3\% malignant versus 8.5\% for non-malignant, p=0.09). Among patients with invasive cancer, 11 (13.3\%) had a short term complication, 31 (37.3\%) had a length of stay greater than 1 day, and 7 procedures were converted to laparotomy (8.4\%). For patients with LOS 0 or 1 day, median BMI was 34.0 and for patients with LOS greater than 1 day, median BMI was 31.5 (p=0.66). When comparing median BMI of patients converted to laparotomy (BMI = 33) and those not converted to laparotomy (BMI = 32) there was no significant difference (p=0.70). Median BMI between patients with a short term complication (BMI=27) versus patients without a short term complication (BMI=33) was also not statistically different (p=0.26). There was no correlation between BMI and LOS (r=-0.017, p=0.88), BMI and case time (r=0.3, p=0.81), or BMI and EBL (r=0.1, p=0.39) or change in hemoglobin (r=-0.06, p=0.57). There was a positive correlation between LOS and patient age (r=0.283, p=0.01). Logistic regression identified that patients with a short term complication were more likely to have an increased LOS (OR 2.71, [95\%CI 1.39-5.29]) but not an increased BMI (OR 0.9, [95\%CI 0.8-1.0]).

Conclusion: Our findings confirm that robotic surgery is a safe option for the obese gynecologic oncology population. Predictably, increasing age and presence of short term complication correlate with increased LOS. Our data show that conversion to laparotomy is not significantly associated with BMI, although this finding is weakened by the small number of cases converted to laparotomy in this study.
Recurrence-free intervals and 5-year survival following robotic-assisted surgical staging for endometrial cancer

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Objective: To report long-term survival and recurrence-free intervals for endometrial cancer patients surgically staged using robotic-assisted laparoscopy.

Methods: Retrospective chart review for all endometrial cancer patients surgically staged with robotic-assisted laparoscopy at the University of North Carolina Hospital. Demographic data, 5-year survival, and recurrence-free intervals were analyzed. Statistical analysis using Chi-square, t-test, and Kaplan-Meier curves were performed with SAS software.

Results: A total of 521 patients were identified and included in the study. Five-year survival was 87.2% after endometrial cancer surgical staging with robotic-assisted laparoscopy. Median follow up time was 22 months, with a range of 0 to 80 months. Recurrence was documented in 9.6% of patients. Among stage IA, IB and II patients, overall survival was 94.1%, 83.5% and 75%, respectively. Tumors with grade 3 histology were more likely to recur when compared with grade 1 and 2 tumors (p<0.0001). Seventy-three percent of patients with grade 3 disease were alive at 5 years in contrast to 92.5 and 94.8% for grade 1 and 2 tumors, respectively. Ninety percent of endometrioid adenocarcinoma patients were alive at five years compared with 75.1% of patients with non-endometrioid adenocarcinoma.

Conclusion: The results in this study demonstrate that robotic-assisted surgical staging for endometrial cancer does not adversely affect survival or rates of recurrence. These findings provide further evidence that robotic-assisted laparoscopic surgical staging is not associated with inferior results when compared to laparotomy or traditional laparoscopy.
Robotic Surgery for the Management of Ovarian Cancer

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Objective: A feasibility study of the use of primary robotic surgery in the treatment of epithelial ovarian and fallopian tube cancer.

Methods: Thirty patients with a preoperative diagnosis of epithelial ovarian/fallopian tube cancer who underwent robotic surgical management between 04/2011-08/2012 were reviewed. Major intraoperative and post operative complications, operative time, blood loss, transfusion rate, length of hospitalization, length of follow up, patient demographics, and ability to optimally debulk and obtain periaortic and pelvic lymph nodes for staging were reviewed.

Results: A total of twenty-eight cases were included in the final analysis. Of the thirty procedures two were aborted secondary to tumor burden and were not included in the final analysis. Two patients had a final surgical pathology of papillary serous adenocarcinoma of the endometrium. There were 19 debulking procedures and 9 staging procedures. There were no major intraoperative complications. No procedures were converted to laparotomy. There were two postoperative complications: one patient had atrial fibrillation on POD#1. Another patient had a small bowel obstruction requiring IV hydration and bowel rest with a nasogastric tube. The mean operative time was 227 minutes. The mean EBL was 74 mL, the mean hemoglobin change was 2.07 g/dL, and the mean hospital stay was 2 days. 94.7% of patients had <1cm tumor residual or no gross residual. 21.4% of cases had neoadjuvant chemotherapy. 64.3% of cases had stage III cancer, 3.6% had stage 4.

Conclusion: Robotic surgery may be feasible for the management of selected women with epithelial ovarian cancer. The presence of advanced stage disease does not appear to be an absolute contraindication to minimally invasive surgery. Even in the setting of radical debulking surgery, minimally invasive surgery may decrease morbidity.
Influence of bevacizumab on vaginal cuff evisceration eight months after ovarian cancer cytoreduction surgery: A case report

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Objective: Antiangiogenic agents, such as bevacizumab, have been shown to inhibit neovascularization by blocking the activity of vascular endothelial growth factor (VEGF). Bevacizumab suppresses tumor growth by initially inducing vessel normalization, and subsequently collapsing vessels leading to hypoxia alone, or in combination with standard chemotherapeutics. Consequently, bevacizumab has been shown to interfere with the healing process and most wound complications have been reported when bevacizumab is given within one month postoperatively. Fewer cases have been reported when the delay between surgical intervention and bevacizumab administration exceeds this one-month window.

Methods: We present a patient receiving bevacizumab starting more than five months after ovarian cancer cytoreduction surgery and experiencing vaginal cuff evisceration at eight plus months postoperatively. The mechanism of action and side effects of bevacizumab will be discussed as they relate to wound healing.

Results: Bevacizumab is suspected of having a key role in causing this complication because of the unusually long passage of time between the surgical intervention and the wound complication, the location of the metastasis at the vaginal cuff, and the potential for delayed wound healing and increased susceptibility to bevacizumab at the vaginal apex.

Conclusions: Treatment of similar metastases with bevacizumab and other antiangiogenic agents in the future warrants close observation even when a significant period of time has passed between surgical intervention and drug administration.
A Cost Comparison after Introducing a Staged Transarterial Embolization and Hysterectomy protocol for Management of Placenta Accreta

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Objective: The placenta accreta spectrum is associated with significant morbidity even appropriate pre-procedure planning has occurred. Our institution previously reported on the effect of introducing a Staged Transarterial Embolization and Hysterectomy (STEH) protocol on patient outcomes. In this study we undertook an analysis of the costs involved in these two approaches.

Methods: Beginning in 2011, cases of prenatally diagnosed placenta accreta were identified and planned cesarean hysterectomies were performed in a hybrid operating room, equipped for both surgery and embolization. Prior to surgery internal iliac balloon catheters were placed and left uninflated. Following delivery select transarterial embolization of the placenta and uterus was carried out. Balloons were inflated, hysterectomy followed, and repeat embolization was performed as needed. We retrospectively retrieved cost and outcome data for all STEH protocol patients and compared them to several historical cases managed conventionally.

Results: Three planned cesarean hysterectomies in 2010 were analyzed against the six STEH cases performed in 2011 and 2012. Patient characteristics were comparable except for higher parity in the conventional cohort (all patients para 4) and presence of 3 histologically-proven percretas in the protocol group (conventional n=0). The mean number of prior abdominal surgeries was higher in the conventional cohort (3.6 versus 2.3). Patients undergoing conventional treatment sustained a higher estimated blood loss (median 9000 mL versus 3250 mL) and were transfused more units of blood (median 22 versus 9). All three conventional patients and one protocol patient required subsequent reoperation via laparotomy for exploration and removal of abdominal packing placed for hemorrhage control at the time of the original surgery. Despite unanimous reoperation, total operative time and anesthesia time were lower for the conventional group (median 4.18 hours and 5.58 hours versus 5.5 hours and 7.58 hours). While operative complications and adverse events during hospitalization were comparable between the two groups, patients undergoing STEH had a shorter median hospital stay (5 days versus 11 days). The overall hospital costs were lower for STEH patients (median $33,342.23 versus $65,785.32). Differences were most pronounced in the areas of room and board (median protocol group $5,488.29 versus $13,101.68), transfusion costs (median protocol group $4,553.04 versus $15,190.15) and pharmacy costs (median protocol group $1,866.43 versus $5,001.13). Costs for radiologic procedures and supplies were comparable (median conventional $10,608.00 and $8,873.83 for STEH patients).

Conclusion: Introduction of a staged embolization and hysterectomy protocol appears to be associated with lower costs for management of placenta accreta when compared to the historical approach.