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Original article

A comparison of outcomes following robotic-assisted staging and laparotomy in patients with early stage endometrioid adenocarcinoma of the uterus with uterine weight under 480 g

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ABSTRACT

Study Objective: To directly compare perioperative morbidity and hospital stay after robotic-assisted staging and laparotomy in patients with early stage endometrial endometrioid adenocarcinoma and uterine weight under 480 g.
Design: Retrospective cohort study.
Setting: The West Clinic in Memphis, TN, USA.
Patients: Patients with Stage IA and Stage IB endometrial endometrioid adenocarcinoma and uterine weight less than 480 g from June 2007 to January 2011.
Interventions: Patients underwent hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection with or without para-aortic lymph node dissection using robotic-assisted surgery or open laparotomy.
Measurements: Perioperative complications and morbidity, length of hospital stay, progression-free survival, overall survival, time to recurrence, and time do death from disease.
Main Results: A total of 160 patients who underwent laparotomy and 165 patients who received robotic-assisted staging were identified. Compared with robotic-assisted staging, laparotomy was associated with increased hospital stay (3 days vs. 1.4 days, $p < 0.001$), greater estimated blood loss (237 cm^3 vs. 102 cm^3, $p < 0.001$), larger uterine weight (136 g vs. 116 g, $p < 0.001$), as well as higher incidence of postoperative complications [29.3% vs. 6.7%, odds ratio (OR) 5.82, 95% confidence interval (CI) 2.1–11.7] including postoperative ileus (9.0% vs. 1.0%, OR 7.82, 95% CI 1.7–35.0), wound infection (6.0% vs. 1.0%, OR 5.43, 95% CI 1.2–25.2), and postoperative atelectasis (4.0% vs. 0%, $p < 0.01$). There were no differences in projected 5-year progression-free and overall survival rates.
Conclusion: Use of the daVinci robotic system was associated with less intraoperative blood loss, fewer postoperative complications, and shorter hospital stay compared with laparotomy for patients with uterine weight less than 480 g.

Introduction

The daVinci robotic surgical system (Intuitive Surgical, Sunnyvale, CA, USA) has had a significant impact on minimally invasive surgical staging for patients with gynecologic malignancies in the

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United States.[1] Retrospective analyses of robotic-assisted staging of endometrial endometrioid adenocarcinoma have demonstrated perioperative and survival outcomes comparable with previously published data for laparoscopic-assisted and open surgical staging.[2–4] Robotic-assisted surgical staging has been adopted by an increasing number of providers as the standard approach for early stage endometrial endometrioid adenocarcinoma.[5] Robotic-assisted staging is now widely used in private gynecologic oncology practices,[6] yet little data about outcomes in private centers exist.

Prior studies comparing laparotomy with minimally invasive surgical techniques have included uterine weights > 500 g,[7] which is associated with an increase in perioperative complications.[8] It has been demonstrated that removing uteri < 480 g vaginally following robotic-assisted hysterectomy with or without vaginal morcellation is both feasible and safe.[9] Given this, we aim to directly compare perioperative outcomes following robotic-assisted staging and laparotomy in patients with early stage endometrial cancer and uterine weight < 480 g.

Materials and Methods

A retrospective chart review was performed for patients who underwent surgical staging for Stage I endometrioid adenocarcinoma of the uterus with postoperative uterine weight < 480 g at the West Clinic from June 2007 to January 2011. The University of Tennessee Health Science Center Institutional Review Board approved this study. Chart review identified 326 patients for analysis. Of these, 166 patients underwent robotic surgical staging and 160 patients received staging by laparotomy. All staging was revised to the International Federation of Gynecology and Obstetrics 2009 classification. Bilateral pelvic lymph node dissection was routinely performed following hysterectomy on all patients. All patients were initially meant to undergo para-aortic lymph node dissection. Obesity during robotic surgery limited para-aortic lymph node dissection in some patients and was omitted. After robotic-assisted or abdominal hysterectomy and bilateral salpingo-oophorectomy were performed, pelvic and para-aortic lymphadenectomy was performed in accordance with the Gynecologic Oncology Group Surgical Procedures Manual. Both the “S” and “Si” models of the daVinci surgical system were used for robotic staging. Lymph nodes were removed through the vagina using a stone grasper. Uteri too large to be removed vaginally were transected using curved Mayo scissors inside an Endo Catch bag (Covidien, Mansfield, MA, USA). Robotic vaginal cuff closure was performed using 2-0 V-Loc (Covidien) in a running fashion. Vaginal cuff closure during open laparotomy was performed using 2.0 VICRYL suture (Ethicon, Cincinnati, OH, USA). Hospital and office charts were retrospectively reviewed for age, body mass index (BMI), estimated blood loss (EBL), depth of myometrial invasion, lymphovascular space invasion, stage, tumor grade, tumor size, uterine weight, adjuvant therapy received, time to disease recurrence, recurrence location, and postoperative complications. Postoperative complications were defined as deep vein thrombosis, pulmonary embolism, pneumonia, ileus, blood transfusion, wound infection, wound evisceration, acute renal injury, atelectasis, and fever requiring readmission within 30 days of surgery. Ileus was defined as nausea and/or emesis requiring nothing by mouth or nasogastric tube placement beyond postoperative Day 2. Hemorrhage was defined as EBL > 500 cm^3 or intraoperative or postoperative blood transfusion within the first 24 hours following surgery. Acute renal injury was defined as an increase in creatinine level by more than two times the preoperative baseline. Statistical analysis using SAS software (SAS Institute Inc., Cary, NC, USA) was performed using Chi-square for discrete variables, *t* test for continuous variables, and Kaplan–Meier curves for disease-free survival. All *t* tests were two sided, and $p < 0.05$ was considered statistically significant.

Results

Table 1 summarizes all patient demographic, surgical, and tumor characteristics. A total 160 patients who underwent laparotomy and 166 patients who underwent robot-assisted staging for both Stage IA and Stage IB endometrioid adenocarcinoma were identified for analysis. There were no significant differences in age ($p = 0.686$), BMI ($p = 0.165$), or tumor size ($p = 0.427$) between the two cohorts. Significantly more pelvic (mean 8.7 ± 7.4 vs. 6.4 ± 4.2, $p = 0.001$) and para-aortic lymph nodes (mean 1.6 ± 2.3 vs. 0.95 ± 1.8, $p = 0.006$) were sampled using laparotomy. Uterine weight was larger for the laparotomy cohort (mean 136 ± 72 g vs. 116 ± 61 g, $p = 0.001$). EBL was higher in patients who underwent laparotomy (mean 237 ± 221 mL vs. 102 ± 103 mL, $p < 0.001$). Patients stayed longer in the hospital following laparotomy than after robotic-assisted staging (3 ± 1.8 days vs. 1.4 ± 1.2 days, $p < 0.0001$). Our conversion rate from robotic-assisted staging to laparotomy was 3.6% (3 for large uterine size, 1 for obesity, 1 for poor pulmonary function in the Trendelenburg position, and 1 for adhesive disease). There were no differences in stage ($p = 0.723$), tumor grade ($p = 0.98$), or presence of lymphatic/vascular space invasion ($p = 0.207$). When comparing those with intermediate risk factors (i.e., Grade 2/3, advanced age, outer third myometrial invasion, or lymphovascular space involvement) there was no difference between the cohorts ($p = 0.966$). One patient who underwent laparotomy and two patients who underwent robotic-assisted staging received adjuvant carboplatin and taxol with concurrent brachytherapy ($p = 0.56$). There were significantly more complications following laparotomy [29.3% vs. 6.7%, odds ratio (OR) 5.82; 95% confidence interval (CI) 2.9–11.7]. Wound infections occurred more frequently after laparotomy (6.0% vs. 1.0%, OR 5.43; 95% CI 1.2–25.2). There was one return to the operating room for abdominal evisceration in the laparotomy cohort. No vaginal eviscerations occurred in either cohort. Postoperative ileus was more common following laparotomy (1.0% vs. 9.0%, OR 7.82; 95% CI 1.7–35.0). Hemorrhage was more likely during laparotomy (4.0% vs. 1.0%, OR 3.73; 95% CI 0.8–18.2). There was no difference in venous thromboembolism rates between the two cohorts ($p = 0.242$; Table 2). Recurrence rates were similar between laparotomy and robotic-assisted staging (10 patients vs. 11 patients, $p = 0.879$, 95% CI −6.0–5.0). The average time to cancer recurrence was similar following robotic-assisted staging and laparotomy (19.4 months and 18.5 months, respectively; $p = 0.865$, 95% CI 9.8–11.5) as was average time to death from endometrial cancer (23.9 months and 22.1 months, respectively; $p = 0.704$, 95% CI −8.9–12.5). There was no difference in disease-related deaths between the two cohorts (4 after laparotomy and 3 following robotic-assisted staging, $p = 0.75$; 95% CI −5.0–3.0; Table 3). There was no difference in projected 5-year progression-free survival following surgical staging between the two cohorts ($p = 0.811$; Figure 1) or projected 5-year overall survival ($p = 0.509$; Figure 2). Sites of recurrence are shown in Table 3. No port-site metastases were noted.

Discussion

Our goal was to directly compare perioperative outcomes for early stage endometrioid adenocarcinoma following robotic-assisted staging and laparotomy in our practice since implementing the daVinci robotic surgical system. We desired to compare outcomes in patients who could have been staged using either surgical modality. Prior studies comparing outcomes following hysterectomy and staging for endometrial cancer have included

Table 1
Patient demographics.

	Open		Robotic assisted		p	95% CI
	N	Mean	N	Mean		
Age (y)	160	64.3 ± 11.8	165	64.8 ± 11.6	0.686	−3.1–2.1
BMI	160	35.5 ± 8.5	165	34.1 ± 9.8	0.166	−0.6–3.4
Pelvic nodes sampled	160	8.7 ± 7.4	165	6.4 ± 4.2	<0.001	0.9–3.6
Aortic nodes sampled	160	1.6 ± 2.3	165	1 ± 1.8	0.006	0.2–1.1
Hospital stay (days)	113	3 ± 1.8	104	1.4 ± 1.2	<0.001	1.2–2.0
EBL (cc)	106	237 ± 221	123	102 ± 103	<0.001	88–181
Tumor size (cm)	159	2.5 ± 2.1	165	2.3 ± 1.9	0.427	0.28–0.66
Uterine weight (g)	160	136 ± 72	165	116 ± 61	0.009	4.8–33.9

	Open		Robotic assisted		p
	N	%	N	%	
Stage					0.763
IA	49	30.6	48	29.1	
IB	111	69.4	117	70.9	
Grade					0.981
1	105	66	110	67	
2	40	25	40	24	
3	15	9	15	9	
Lymphovascular space invasion	5	3	10	6	0.207
Gynecologic Oncology Group 99 intermittent risk criteria					0.966
Low risk	98	61	100	61	
Low intermittent risk	34	21	37	22	
High intermittent risk	28	18	28	17	
Adjuvant treatment received	24	15	17	10	0.202
Chemotherapy + radiation	1	4	2	12	0.560
Radiation alone	23	96	15	88	

BMI = body mass index; CI = confidence interval; EBL = estimated blood loss.

Table 2
Perioperative complications.

	Open		Robotic assisted		p	95% CI	Odds ratio
	N	%	N	%			
Total complications	47	29.3	11	6.7	<0.001	2.9–11.7	5.82
DVT	2	1.3	0	0.0	0.242	—	—
PE	1	1.0	1	1.0	>0.99	0.1–16.6	1.03
Pneumonia	2	1.0	1	1.0	0.618	0.2–23.1	2.08
Ileus	14	9.0	2	1.0	0.002	1.7–35.0	7.82
Bowel obstruction	2	1.0	0	0.0	0.242	—	—
Hemorrhage	7	4.0	2	1.0	0.1	0.8–18.2	3.73
Wound infection	10	6.0	2	1.0	0.016	1.2–25.2	5.43
Intraoperative injury[a]	2	1.0	0	0.0	0.242	—	—
Atelectasis	6	4.0	0	0.0	0.014	—	—
Bladder atony	1	1.0	2	1.0	>0.99	0.05–5.7	0.51
Renal failure	0	0.0	1	1.0	>0.99	—	—

CI = confidence interval; DVT = deep vein thrombosis; PE = pulmonary embolus.
[a] One intraoperative enterotomy and one intraoperative ureteral injury.

Table 3
Disease-related survival characteristics.

	Open		Robotic assisted		p
	N	%	N	%	
Recurrences	10	6	11	7	0.879
Deaths from disease	4	3	6	4	0.75

	N	Mean	N	Mean	p
Average months to recurrence	10	19.4	10	18.5	0.865
Average months to death	4	23.9	6	22.1	0.704

	Open (%)	Robotic assisted (%)	p
Projected 5-y PFS	93	92	0.8112
Projected 5-y OS	97	96	0.5094

OS = overall survival; PFS = progression-free survival.

uteri too large to be removed vaginally following robotic-assisted staging. We chose to directly compare outcomes in patients who could have been staged using either surgical modality. Multiple centers have shown transvaginal removal of uteri with a mean weight of > 480 g to be feasible.[9] Given this, we chose 480 g as our cutoff for analysis. We also desired to compare outcomes associated with the use of minimally invasive staging for early stage endometrioid adenocarcinoma of the uterus at our practice with those reported in trials, predominantly performed at large, fellowship-associated, academic centers.[2–4] We limited our analysis to patients with Stage I endometrial cancer as this comprised the majority of our patient population and a disproportionate number of patients in Stages II–IV were staged using laparotomy. Although a comparison between laparoscopic, robotic, and open approaches to endometrial cancer staging would be useful, none of the surgeons

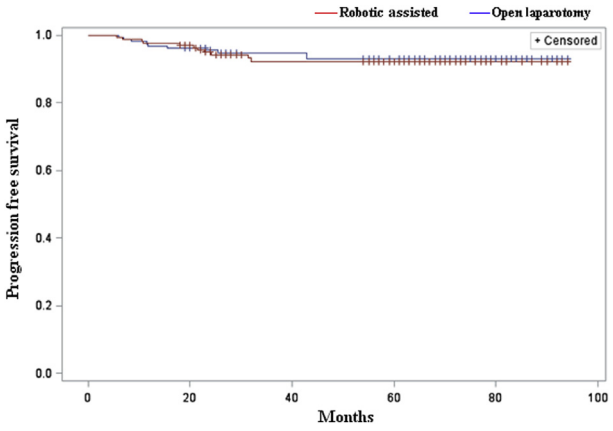

Figure 1. Projected 5-year survival curve.

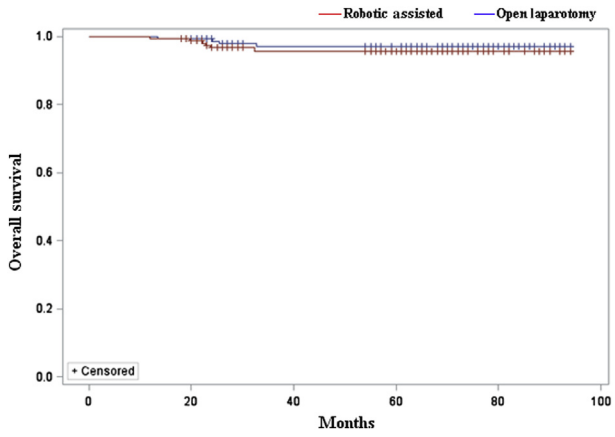

Figure 2. Projected 5-year overall survival curve.

at our institution perform laparoscopic staging for endometrial cancer.

Our perioperative outcomes following both laparotomy and robot-assisted staging were similar to those reported from large academic institutions. Gaia et al[4] performed a systemic review of five comparative studies between laparotomy and robotic-assisted staging of endometrial cancer. In their study, robotic-assisted staging was associated with an average EBL of 101 mL and average length of hospital stay (LOS) of 1.2 days. Laparotomy was associated with an average EBL of 291 mL and average LOS of 3.9 days. Our LOS for robotic-assisted staging (1.4 days) and laparotomy (3 days) and EBL during robotic-assisted staging (103.8 mL) and laparotomy (246 mL) were similar to the comparative data reported by Gaia et al.[4] The overall postoperative complication (6.7% robotic and 29.3% laparotomy) and wound infection (1.2% robotic and 6.2% laparotomy) rates were similar to other reports from predominantly academic centers.[7,10,11] Lastly, our rate of conversion from robotic-assisted staging to laparotomy was similar to previously published studies.[12]

Although our study was not powered for survival analysis, we found no difference in relapse-free survival or time to recurrence between the robotic-assisted and laparotomy cohorts. The two cohorts were similar in stage, tumor grade and size, depth of invasion, and presence of lymphovascular space invasion. Both cohorts were also similar in adjuvant therapy received. Recurrence-free survival of early stage endometrial endometrioid adenocarcinoma was similar to data from previous retrospective studies comparing robotic-assisted staging with laparotomy at 3 years (89.3% and 85.2%),[2,3] as well as that found in LAP2 (89.8%).[13] There was also no difference in disease-specific survival between the two cohorts, similar to previously published data on 3-year disease-specific survival following robotic-assisted staging, which were 92.5% and 94.2%, respectively.[2,3] Our projected 5-year progression-free (92%) and overall survival (97%) following robotic-assisted were also similar to previously published data.[3]

One of the major differences between our results and previously published studies comparing robotic-assisted staging with laparotomy was the number of lymph nodes sampled. In their comparative study, Gaia et al[4] reported a nonsignificant increase in pelvic and para-aortic lymph node yield by robotic-assisted staging compared with laparotomy (18.0 vs. 14.5 and 9.4 vs. 5.7, respectively). Compared with the data from larger academic institutions,[7] less number of pelvic and periaortic nodes were sampled from both staging modalities in this study; laparotomy resulted in higher yields for both pelvic nodes (8.4 vs. 6.2, $p = 0.003$) and periaortic nodes (1.6 vs. 0.95, $p = 0.002$) compared with robotic-assisted staging. The low lymph node yield is interesting given the data from our clinic published in 2009 showing a pelvic lymph node count of 17.8/patient when sent separately to pathology as common iliac, external iliac, internal iliac, and obturator nodes, a practice we have continued.[14] Although age and BMI can be a determinant in the lymph node count,[15] both the average BMI and age of our patients were similar for patients staged robotically and by laparotomy. Despite the fact that the lymph node count differed between prior studies and modalities, it did not affect relapse-free or overall survival in our population.

The costs associated with robotic, laparoscopic, and abdominal hysterectomy have been studied extensively. While robotic hysterectomy has been shown to be less costly than abdominal hysterectomy in multiple studies,[6,16] we believe the true cost–benefit lies in the decreased complications associated with robotic hysterectomy compared with an abdominal approach. Our data show that abdominal hysterectomy significantly increases postoperative ileus, wound infection, and blood loss of > 500 mL. Postoperative ileus significantly increases hospital costs by > $8000 in patients who underwent colectomy.[17] According to a Centers for Disease Control and Prevention estimate, the average costs of surgical site infection ranges between $10,443 and $25,546.[18] Lastly, blood loss and transfusion are associated with increased surgical costs.[19] Given the significant costs of the morbidity associated with abdominal hysterectomy, an analysis of cost, including surgical complications, may further widen the cost difference between the two approaches. Laparoscopic surgical staging of endometrial cancer is associated with the least cost and a similar complication rate but we were not able to include this in our analysis as no surgeons perform laparoscopic staging at our institution.[16]

The strengths of our study are the ability to directly compare both short- and long-term outcomes, uniformity of adjuvant treatment and surgical protocols, treatment at a single institution, and the relatively large number of patients. Our main weakness is the retrospective nature of this study. Complications may not have been documented in discharge summaries, operative reports, or office notes; or simply not scanned into office records. We practice at two different hospital systems that used paper medical records until 2007 and now use different electronic medical records systems, which have changed over the past few years. This made us mainly reliant on records that were scanned into our electronic medical system in our office at the time of surgery or treatment. We also did not collect data on quality of life, return to activities of daily living, or return to work following hysterectomy, where we feel the true benefit of minimally invasive surgery lies.

This study confirms the well-documented excellent perioperative outcomes following robotic-assisted staging and also contributes to a growing body of literature providing further evidence that robotic-assisted staging is not associated with inferior relapse-free and overall survival compared with laparotomy. Furthermore, our data confirm that significantly less intraoperative EBL, shorter LOS, less postoperative complications, and fewer wound infections following robotic-assisted staging for early stage endometrial adenocarcinoma occur in a private practice setting.

References

1. Ramirez PT, Adams S, Boggess JF, Burke WM, Frumovitz M, Gardner GJ, et al. Robotic-assisted surgery in gynecologic oncology: a Society of Gynecologic Oncology Consensus Statement. Developed by the Society of Gynecologic Oncology's Clinical Practice Robotics Task Force. *Gynecol Oncol.* 2012;124:180–184.
2. Kilgore JE, Jackson AL, Ko EM, Soper JT, Van Le L, Gehrig PA, et al. Recurrence-free and 5-year survival following robotic-assisted surgical staging for endometrial carcinoma. *Gynecol Oncol.* 2013;123:49–53.

3. Cardenas-Goicoechea J, Shepherd A, Momeni M, Mandeli J, Chuang L, Gretz H, et al. Survival analysis of robotic versus traditional laparoscopic surgical staging for endometrial cancer. *Am J Obstet Gynecol*. 2014;210:160.e1–160.e11.
4. Gaia G, Holloway RW, Santoro L, Ahmad S, Di Silverio E, Spinillo A. Robotic-assisted hysterectomy for endometrial cancer compared with traditional laparoscopic and laparotomy approaches: a systematic review. *Obstet Gynecol*. 2010;116:1422–1431.
5. Verheijen R, Zweemer R. Robotic surgery for gynaecologic cancer: an overview. *Curr Oncol Rep*. 2012;14:544–549.
6. Yu X, Lum D, Kiet TK, Fuh KC, Orr Jr J, Brooks RA, et al. Utilization of and charges for robotic versus laparoscopic versus open surgery for endometrial cancer. *J Surg Oncol*. 2014;107:653–658.
7. Boggess JF, Gehrig PA, Cantrell L, Shafer A, Ridgway M, Skinner EN, et al. A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: robotic assistance, laparoscopy, laparotomy. *Am J Obstet Gynecol*. 2008;199:360.e1–360.e9.
8. Bonilla DJ, Mains L, Whitaker R, Crawford B, Finan M, Magnus M. Uterine weight as a predictor of morbidity after a benign abdominal and total laparoscopic hysterectomy. *J Reprod Med*. 2007;52:490–498.
9. Payne TN, Dauterive FR, Pitter MC, Giep HN, Giep BN, Grogg TW, et al. Robotically assisted hysterectomy in patients with large uteri: outcomes in five community practices. *Obstet Gynecol*. 2010;115:535–542.
10. Bell MC, Torgerson J, Seshadri-Kreaden U, Suttle AW, Hunt S. Comparison of outcomes and cost for endometrial cancer staging via traditional laparotomy, standard laparoscopy and robotic techniques. *Gynecol Oncol*. 2008;111:407–411.
11. DeNardis SA, Holloway RW, Bigsby 4th GE, Pikaart DP, Ahmad S, Finkler NJ. Robotically assisted laparoscopic hysterectomy versus total abdominal hysterectomy and lymphadenectomy for endometrial cancer. *Gynecol Oncol*. 2008;111:412–417.
12. ElSahwi KS, Hooper C, De Leon MC, Gallo TN, Ratner E, Silasi DA, et al. Comparison between 155 cases of robotic vs. 150 cases of open surgical staging for endometrial cancer. *Gynecol Oncol*. 2012;124:260–264.
13. Walker JL, Piedmonte MR, Spirtos NM, Eisenkop SM, Schlaerth JB, Mannel RS, et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *J Clin Oncol*. 2012;30:695–700.
14. Santoso JT, Azadi A, Wan J, Handorf C, Coleman RL, Tillmanns TD. Lymph node counts in uterine cancer: a randomized double blind trial. *Gynecol Oncol*. 2009;113:159–162.
15. Hareyama H, Ito K, Watanabe S, Hakoyama M, Uchida A, Oku K, et al. Factors influencing the number of pelvic and para-aortic lymph nodes removed in surgical treatment of endometrial and ovarian cancer. *Int J Gynecol Cancer*. 2012;22:1577–1584.
16. Zakhari A, Czuzoj-Shulman N, Spence AR, Gotlieb WH, Abenhaim HA. Laparoscopic and robot-assisted hysterectomy for uterine cancer: a comparison of costs and complications. *Am J Obstet Gynecol*. 2015. http://dx.doi.org/10.1016/j.ajog.2015.07.004.
17. Asgeirsson T, El-Badawi KI, Mahmood A, Barletta J, Luchtefeld M, Senagore AJ. Postoperative ileus: it costs more than you expect. *J Am Coll Surg*. 2010;210:228–231.
18. Scott II RD. *The Direct Medical Costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention*. Atlanta, GA: Division of Healthcare Quality Promotion, National Center for Preparedness, Detection and Control of Infectious Diseases Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention; 2009.
19. Stokes ME, Ye X, Shah M, Mercaldi K, Reynolds MW, Rupnow MF, et al. Impact of bleeding-related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. *BMC Health Serv Res*. 2011;11:135.